

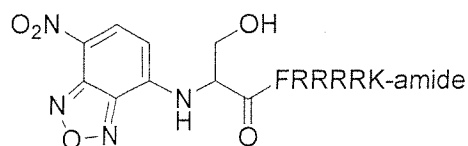
Applicant: David S. Lawrence
Serial No.: 10/755,086
Filed: January 9, 2004
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Amendments to the Claims:

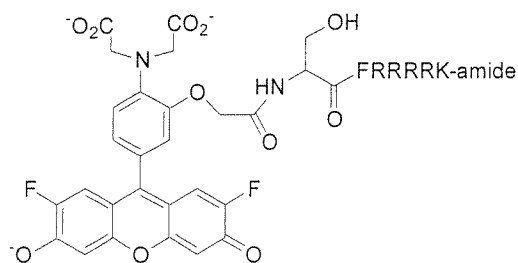
Please cancel Claim 98 without prejudice or disclaimer, and amend Claims 49, 60-66, 80, 88-90, 93, 99, 101, 127-129, 148 and 153 as set forth below.

1-48. (Canceled)

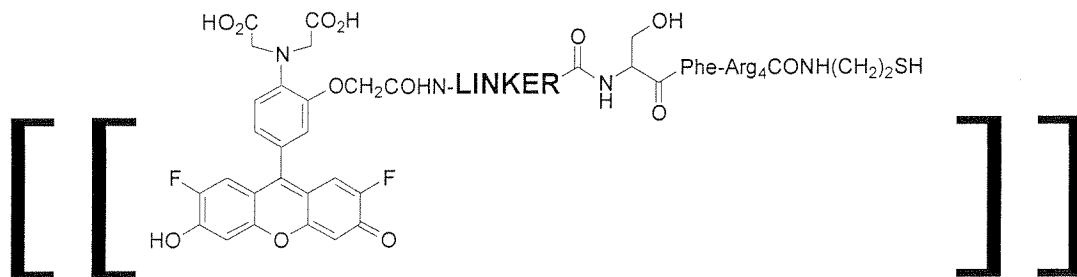
49. (Currently amended) A substrate for a protein kinase, wherein the substrate is selected from the group consisting of:

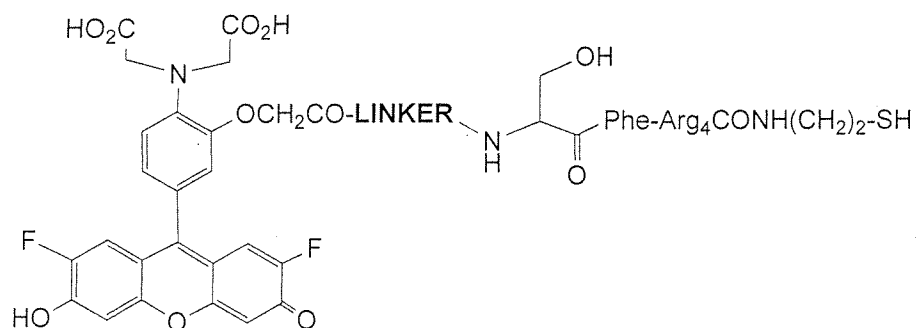


(SEQ ID NO:3),



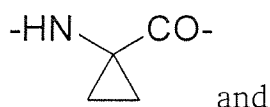
(SEQ ID NO:3), and



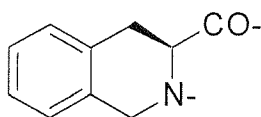


(SEQ ID NO:1);

wherein F is phenylalanine, K is lysine, and R is arginine; and wherein the LINKER is selected from the group consisting of N-methyl glycine, L-proline, D-proline,



and



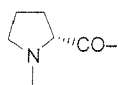
50-55. (Canceled)

56. (Previously presented) A substrate for a protein kinase or a precursor of the substrate, wherein the substrate or the precursor comprises:

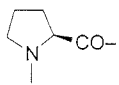
a peptide substrate for the protein kinase, wherein the peptide comprises a serine, a threonine, or a tyrosine on a terminal end of the peptide;

at least one fluorophore, wherein a fluorophore is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide;

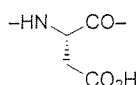
wherein the fluorophore is attached to the peptide by a linker selected from the group consisting of



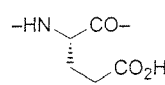
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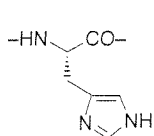
b



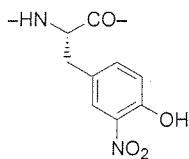
c



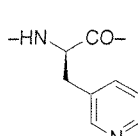
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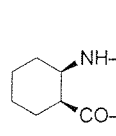
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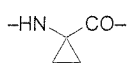
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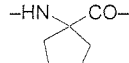
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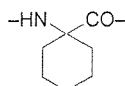
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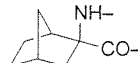
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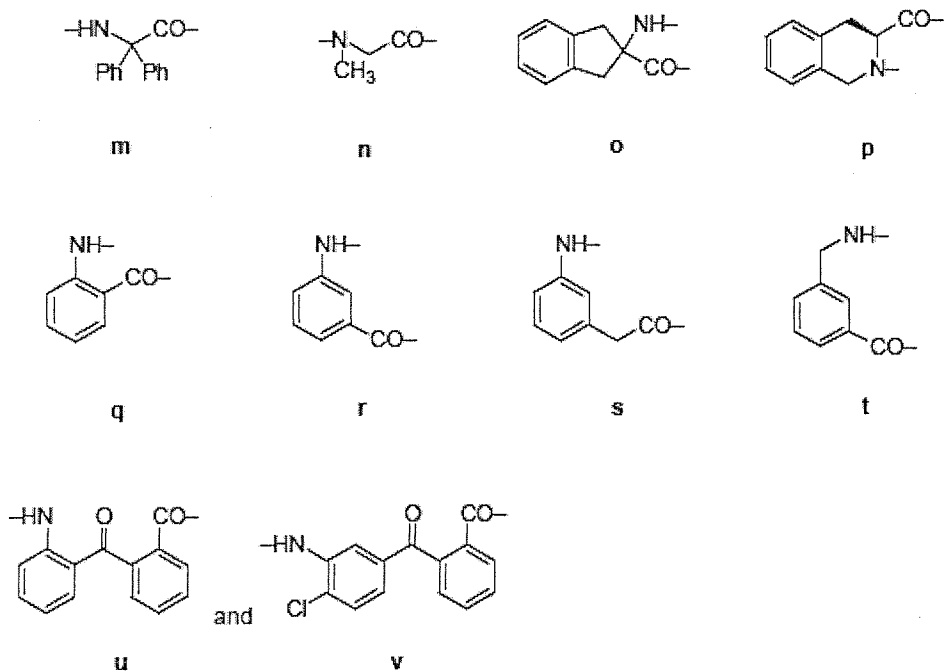
j



k



l

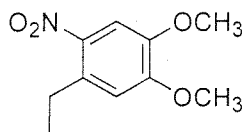


; and

wherein

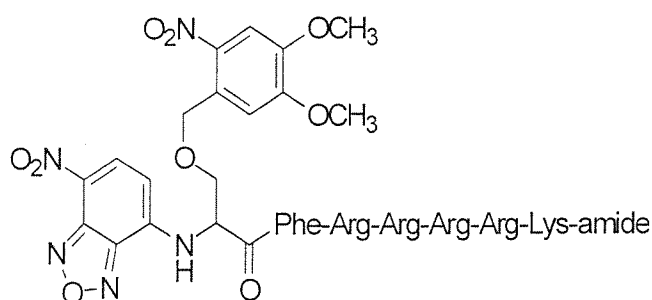
- (i) the substrate is specific for a protein kinase subtype,
- (ii) the fluorophore is attached to the C-terminal end of the peptide,
- (iii) a fluorophore is attached to each terminal end of the peptide,
- (iv) a first fluorophore is attached to a terminal end of the peptide and a second fluorophore, with photophysical properties distinct from the first fluorophore, is attached to any nonterminal site on the peptide,
- (v) the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative, and/or
- (vi) the substrate further comprises a carbohydrate, a lipid or a nucleic acid.

57. (Previously presented) The precursor of the substrate of claim 148, wherein the photolabile side chain comprises the structure



58. (Previously presented) The precursor of the substrate of claim 56, wherein the precursor of the substrate comprises a serine with a photolabile side chain that blocks phosphoryl transfer.

59. (Previously presented) The precursor of a substrate for a protein kinase, where the precursor comprises SEQ ID NO:3 and has the structure



60. (Currently amended) The precursor of a substrate for a protein kinase ~~substrate or the precursor of the substrate~~ of claim 148, wherein after removal of the photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces at least a 20% change in fluorescence intensity.

61. (Currently amended) The precursor of a substrate for a protein kinase ~~substrate or the precursor of the substrate~~ of claim 148, wherein after removal of the

photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces at least a 20% increase in fluorescence intensity.

62. (Currently amended) The precursor of a substrate for a protein kinase ~~substrate or the precursor of the substrate~~ of claim 148, wherein after removal of the photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces at least a 20% decrease in fluorescence intensity.

63. (Currently amended) The precursor of a substrate for a protein kinase ~~substrate~~ of claim 60, wherein phosphorylation ~~of the substrate~~ by the protein kinase produces at least a 70% change in fluorescence intensity.

64. (Currently amended) The precursor of a substrate for a protein kinase ~~substrate~~ of claim 63, wherein phosphorylation ~~of the substrate~~ by the protein kinase produces at least a 100% change in fluorescence intensity.

65. (Currently amended) The precursor of a substrate for a protein kinase ~~substrate~~ of claim 64, wherein phosphorylation ~~of the substrate~~ by the protein kinase produces at least a 150% change in fluorescence intensity.

66. (Currently amended) The precursor of a substrate for a protein kinase ~~substrate~~ of claim 65, wherein phosphorylation ~~of the substrate~~ by the protein kinase produces at least a 250% change in fluorescence intensity.

67. (Previously presented) The substrate of claim 56, wherein the substrate is specific for a protein kinase subtype.

68. (Original) The substrate of claim 67, wherein the substrate is specific for protein kinase C.

69. (Original) The substrate of claim 68, wherein the substrate is specific for isoforms α , β , and γ of protein kinase C.

70. (Original) The substrate of claim 67, wherein the substrate is specific for protein kinase A, protein kinase B, protein kinase D, protein kinase G, Ca^{+} /calmodulin-dependent protein kinase, mitogen-activated protein kinase, protein kinase mos, protein kinase raf, protein tyrosine kinase, tyrosine kinase abl, tyrosine kinase src, tyrosine kinase yes, tyrosine kinase fps, tyrosine kinase met, cyclin-dependent protein kinase, or cdc2 kinase.

71. (Previously presented) The substrate or the precursor of the substrate of claim 56, wherein the substrate further comprises a carbohydrate, a lipid or a nucleic acid.

72. (Canceled)

73. (Previously presented) The substrate or the precursor of the substrate of claim 56, wherein the fluorophore is attached to the C-terminal end of the peptide.

74. (Previously presented) The substrate or the precursor of the substrate of claim 56, wherein the fluorophore is attached to the N-terminal end of the peptide.

75. (Previously presented) The substrate or the precursor of the substrate of claim 56, wherein a fluorophore is attached to each terminal end of the peptide.

76. (Previously presented) The substrate or the precursor of the substrate of claim 75, wherein fluorophores with distinct photophysical properties are attached to different terminal ends of the peptide.

77. (Previously presented) The substrate or the precursor of the substrate of claim 56, wherein a first fluorophore is attached to a terminal end of the peptide and a second fluorophore, with photophysical properties distinct from the first fluorophore, is attached to any nonterminal site on the peptide.

78. (Previously presented) The substrate or the precursor of the substrate of claim 56, wherein the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative.

79. (Previously presented) The substrate or the precursor of the substrate of claim 56, wherein the fluorophore comprises a fluorescein group.

80. (Currently amended) The substrate or the precursor of the substrate of claim 56, wherein the fluorophore comprises a dansyl group, an acridine group, an Alexa Fluor \oplus group, a BODIPY \oplus group, an Oregon Green \oplus group, a Rhodamine Green group, a Rhodamine Red-X group, a Texas Red \oplus group, a Cascade Blue \oplus group, a Cascade Yellow group, a Marina Blue \oplus group, a Pacific Blue group, an AMCA-X group, or a coumarin group.

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81-82. (Canceled)

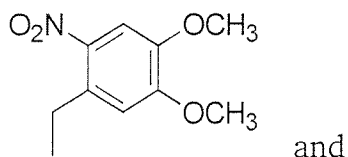
83. (Previously presented) A precursor for a substrate for a protein kinase, wherein the precursor for the substrate comprises:

a peptide comprising a serine, a threonine, or a tyrosine on a terminal end of the peptide;

at least one fluorophore, wherein a fluorophore is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide; and

a photolabile side chain attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide, wherein the photolabile side chain blocks transfer of a phosphoryl group from adenosine triphosphate to a hydroxyl moiety of the serine, the threonine, or the tyrosine so that the substrate cannot be phosphorylated by a protein kinase until the photolabile side chain is removed from the substrate, and

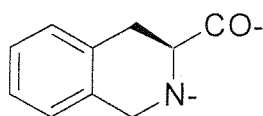
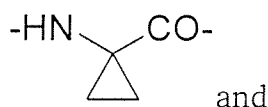
wherein the the photolabile side chain comprises the structure



wherein the fluorophore is attached to the peptide by a linker selected from the group consisting of a carboxamide linker, an aminobenzoic acid linker, a sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an alkylamine linker, an arylamine linker, an ether linker, and a thioether linker.

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84. (Previously presented) The substrate or the precursor for the substrate of claim 56, wherein the fluorophore is attached to the peptide by a linker selected from the group consisting of N-methyl glycine, L-proline, D-proline,



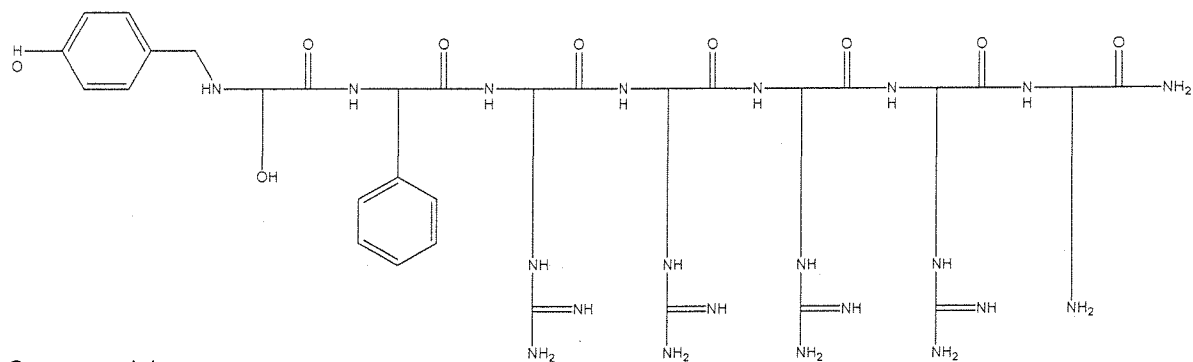
85. (Canceled)

86. (Previously presented) A composition comprising the substrate or the precursor for the substrate of claim 56, and a carrier.

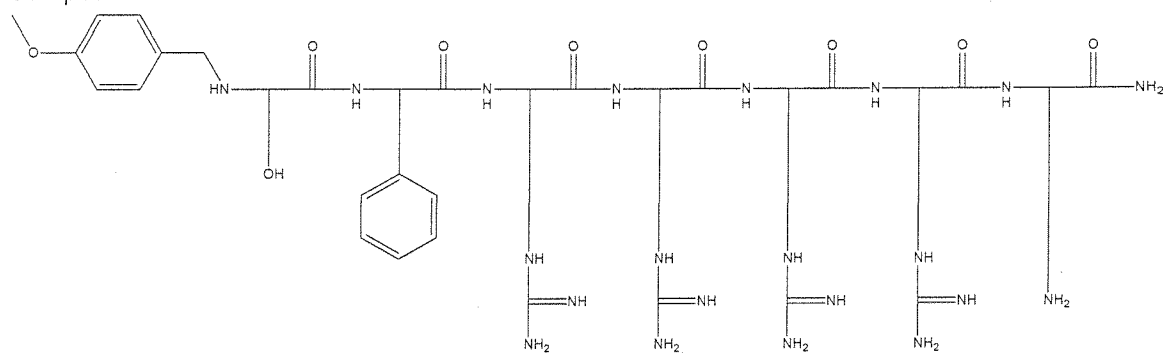
87. (Original) The composition of claim 86, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

88. (Currently amended) A chemical compound comprising ~~SEQ ID NO:3~~ selected from the group of compounds consisting of:

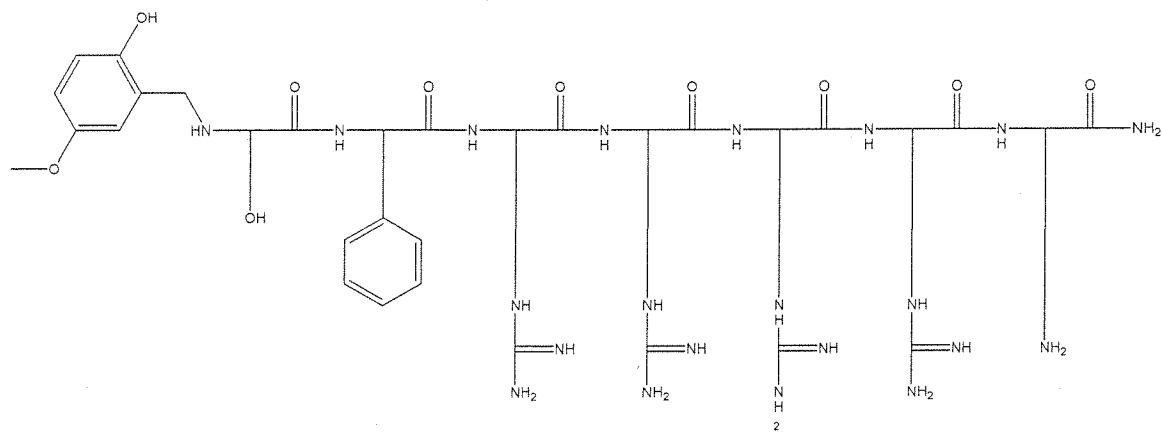
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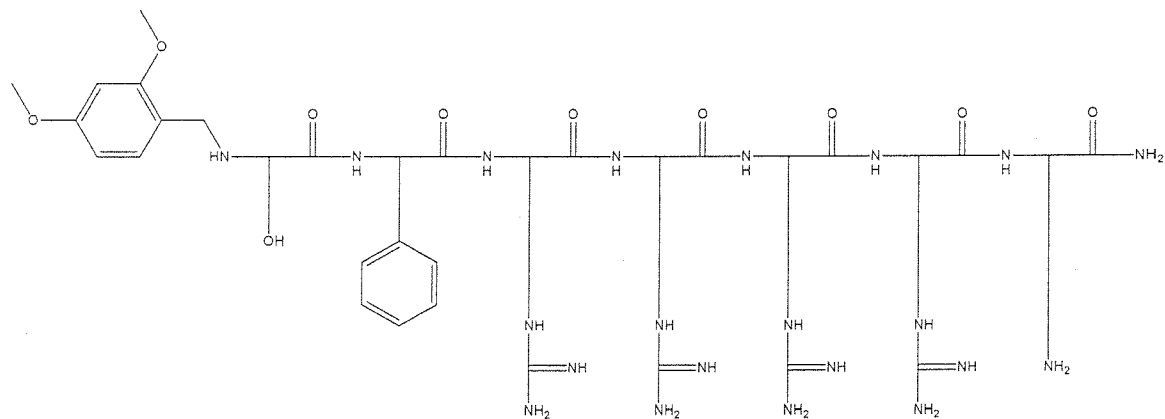
Compound 1



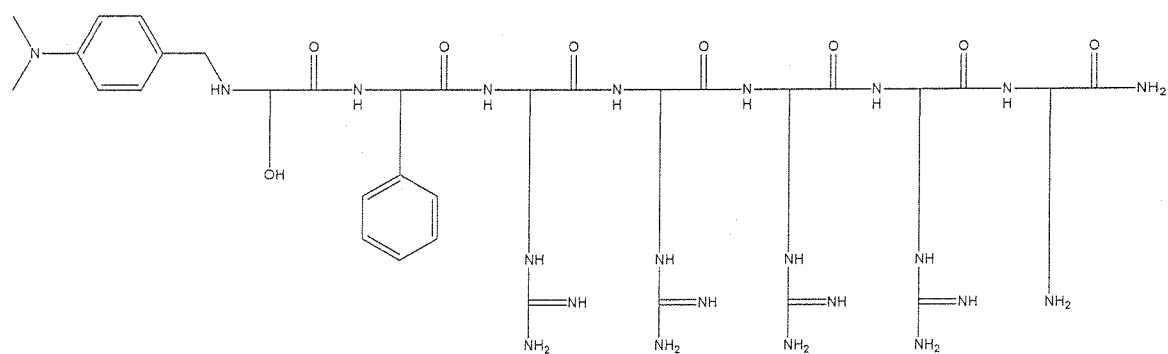
Compound 2



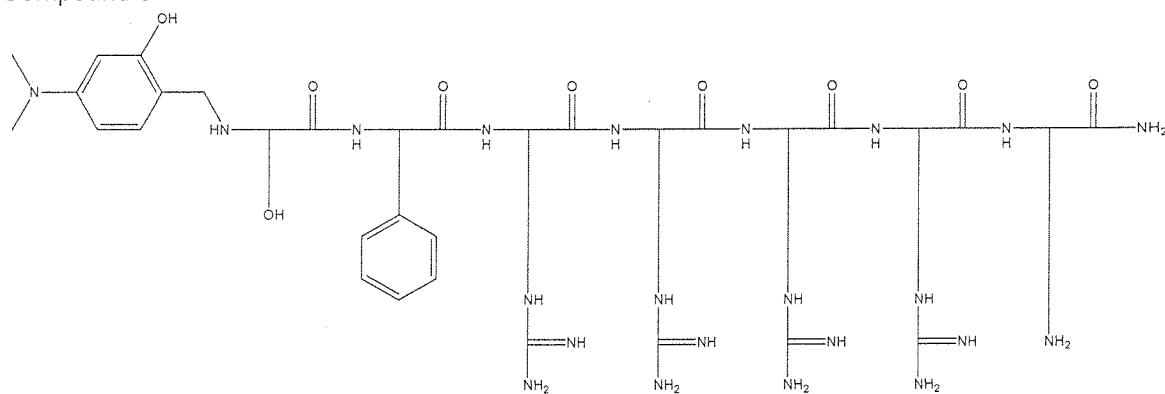
Compound 3



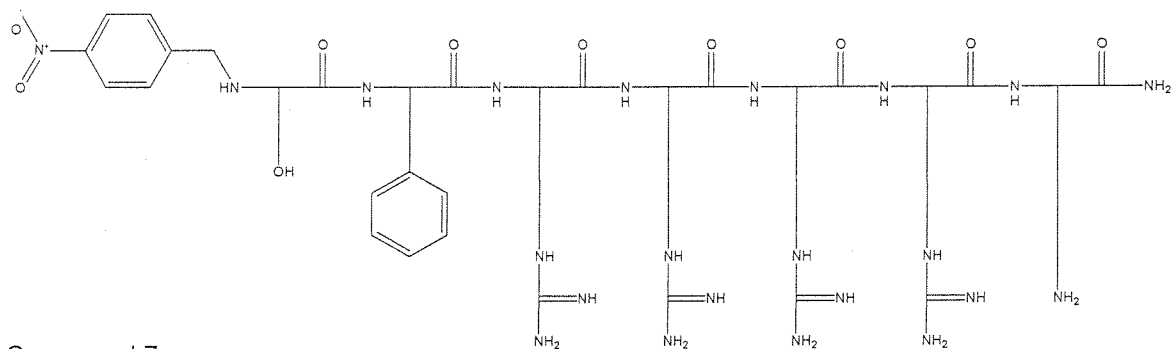
Compound 4



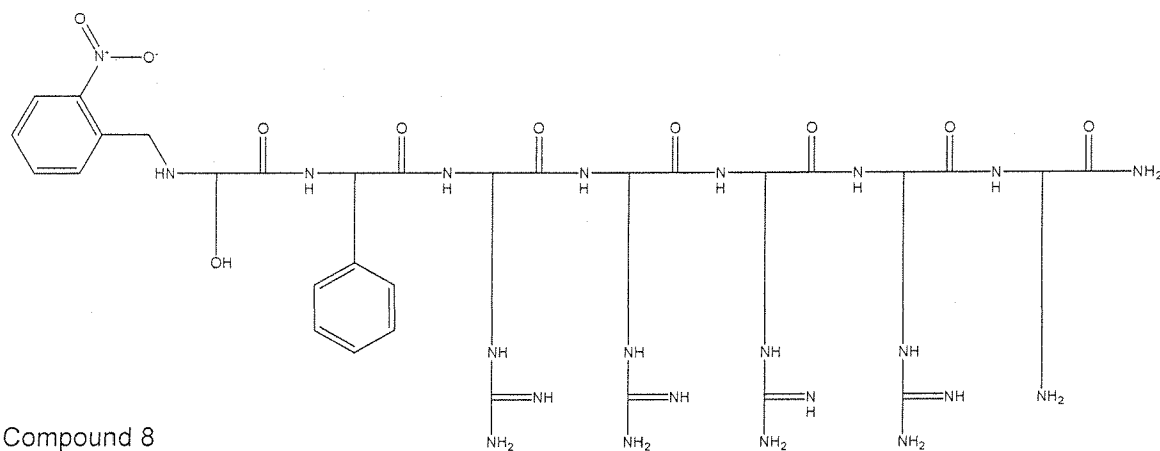
Compound 5



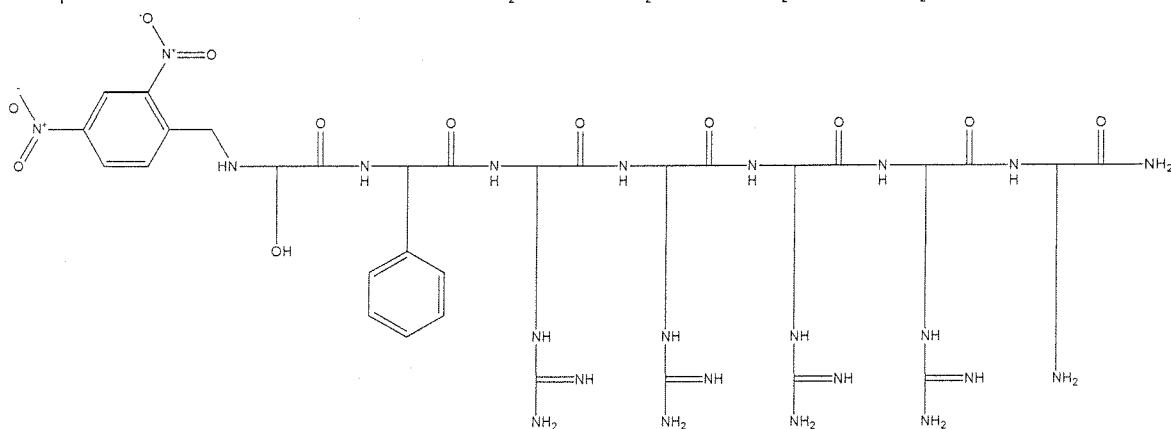
Compound 6



Compound 7



Compound 8



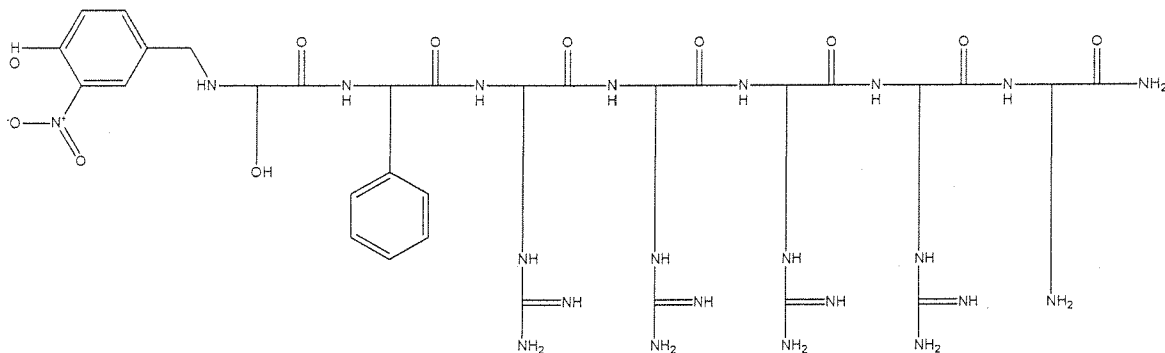
Compound 9

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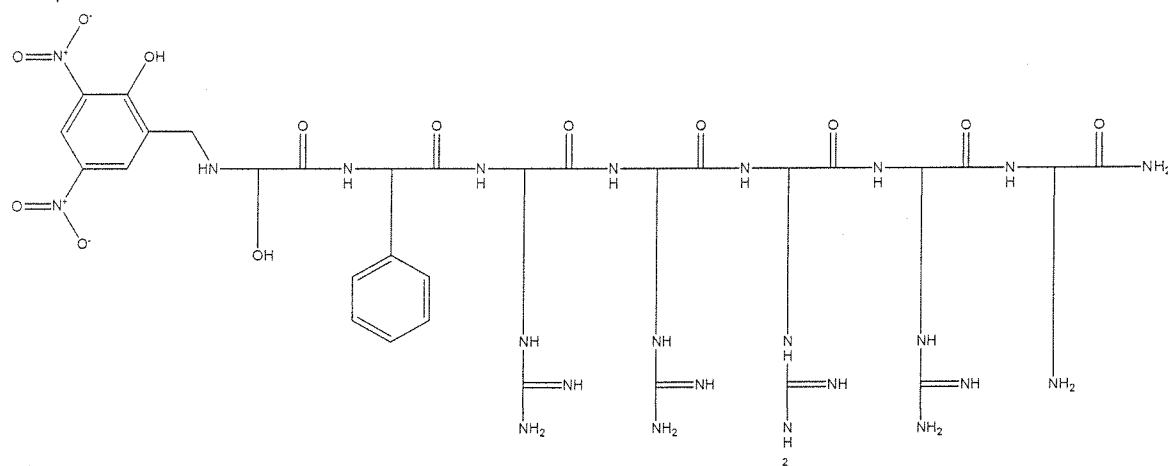
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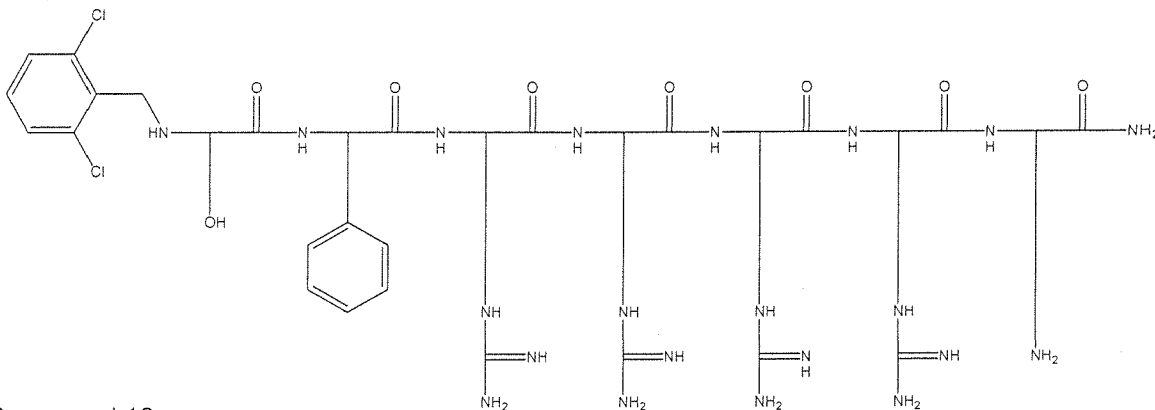
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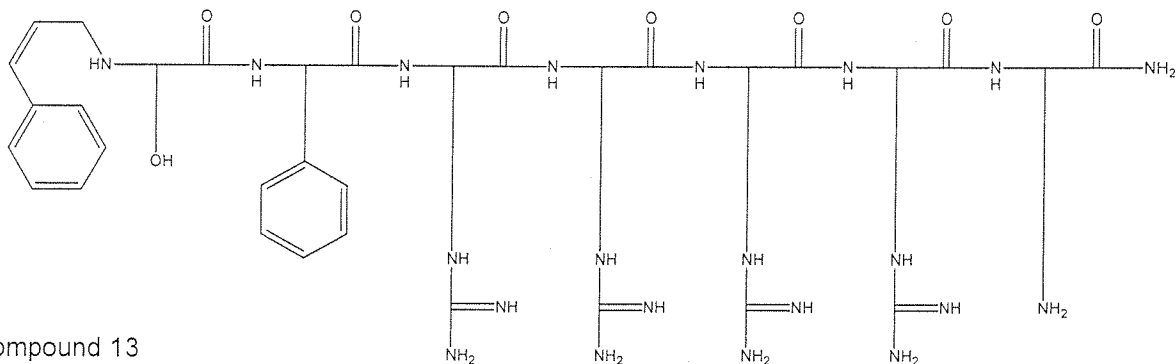
Compound 10



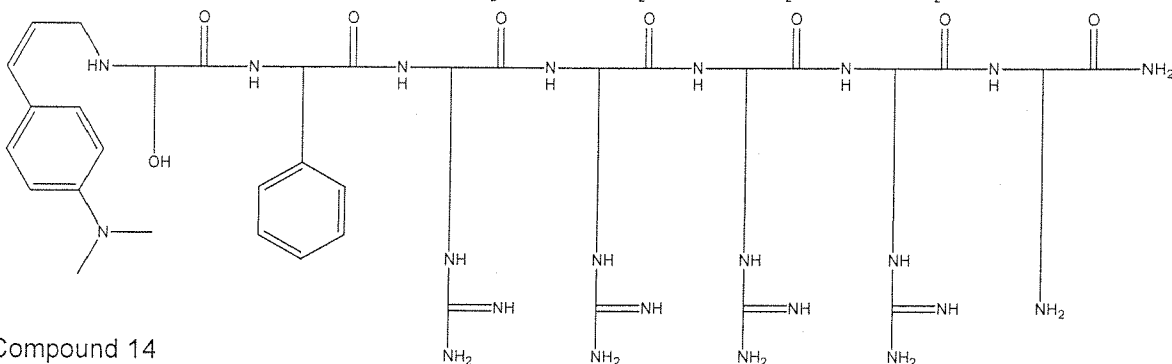
Compound 11



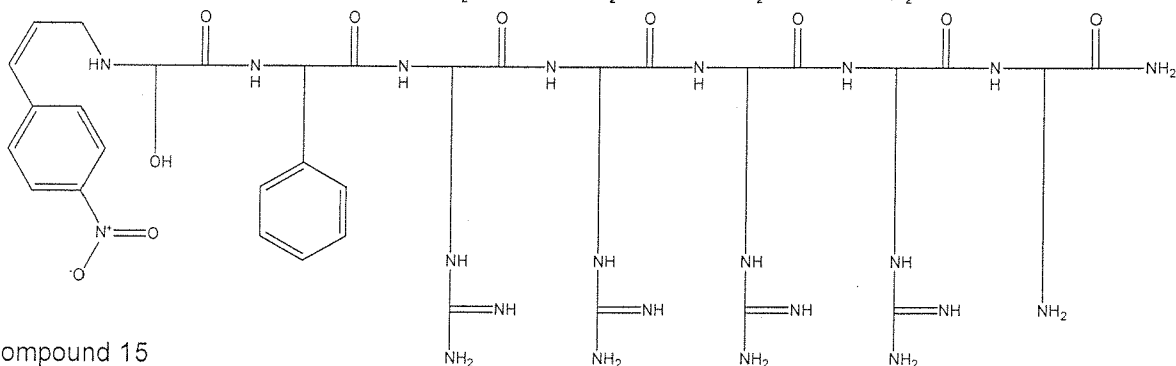
Compound 12



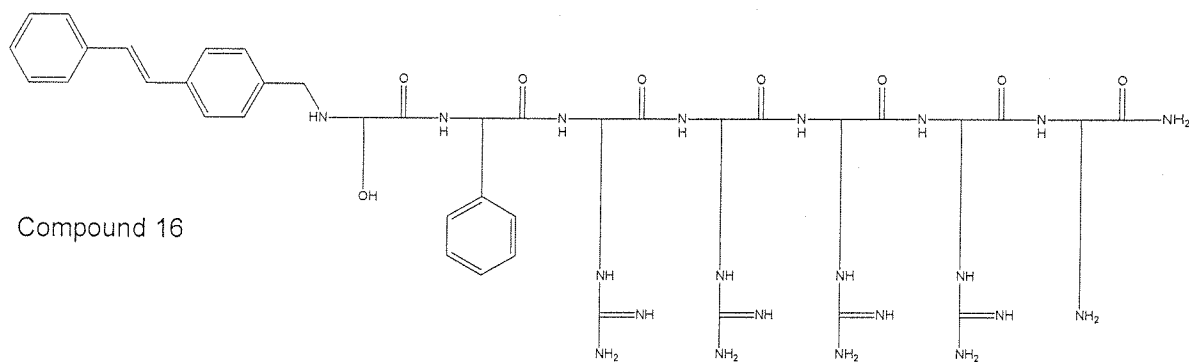
Compound 13



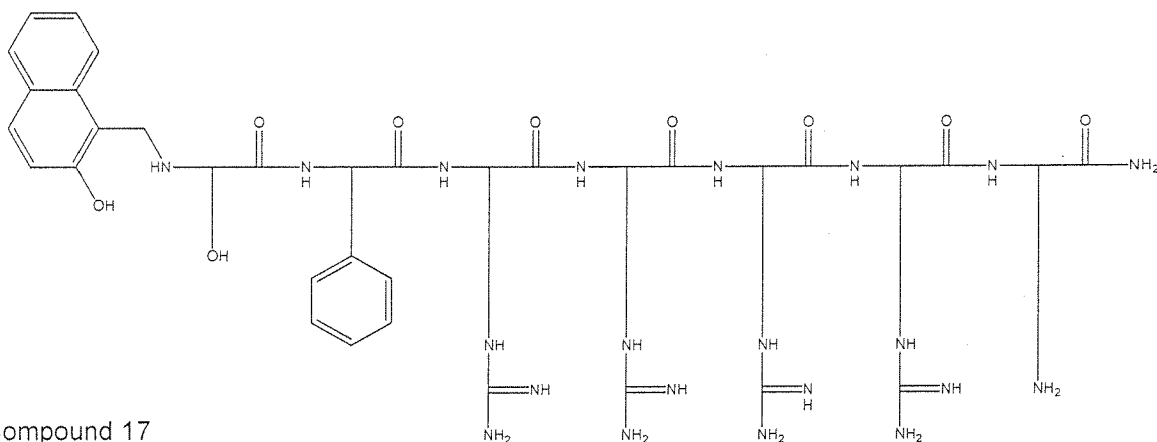
Compound 14



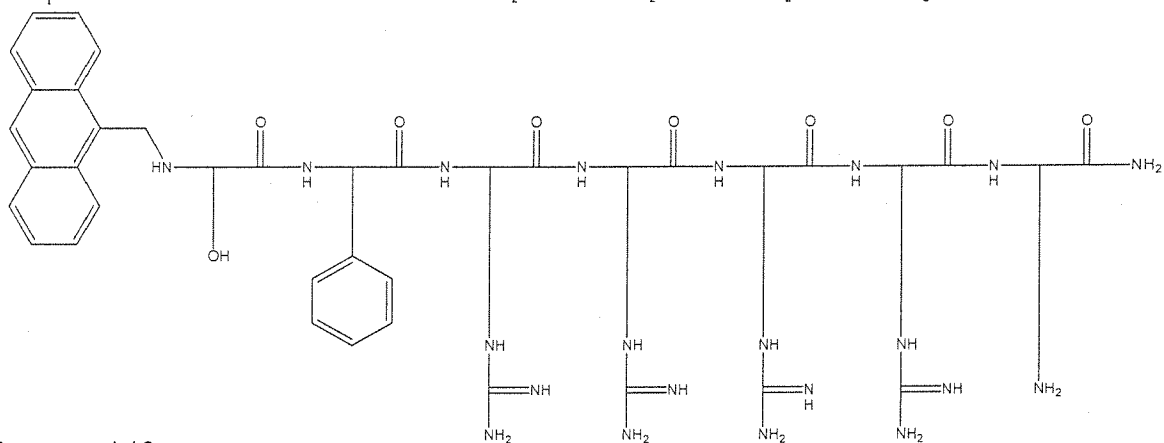
Compound 15



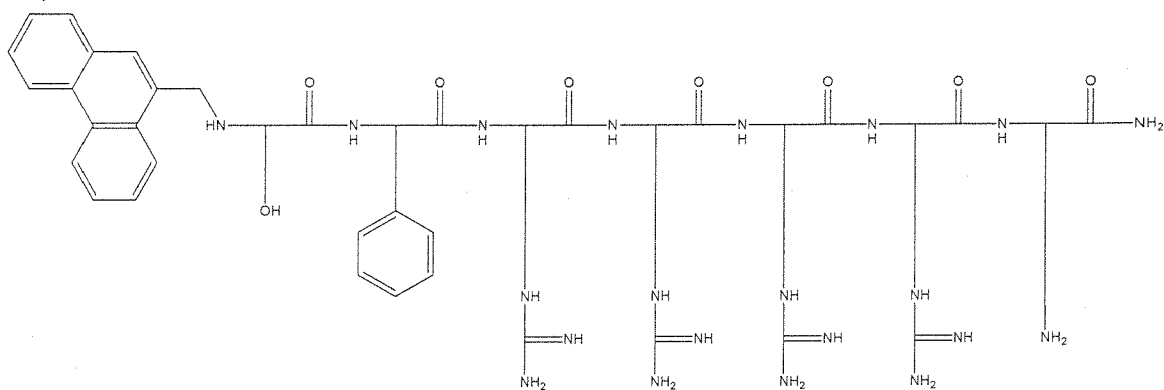
Compound 16



Compound 17

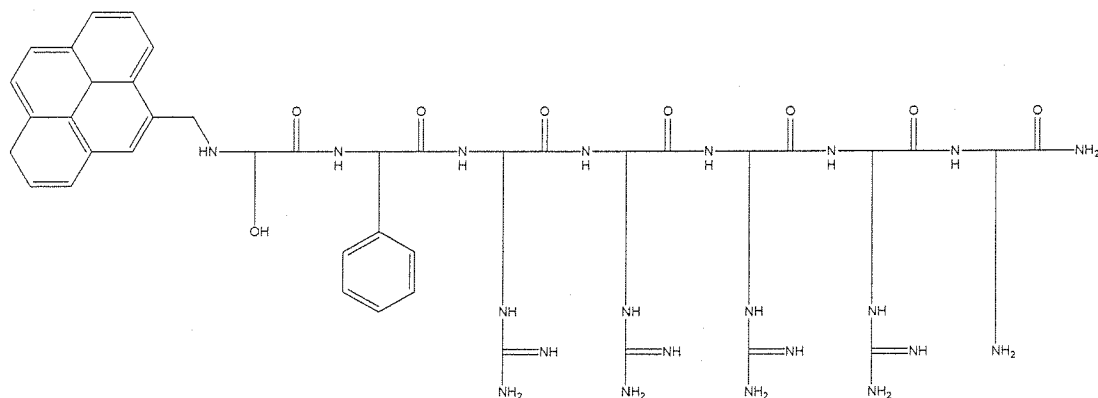


Compound 18

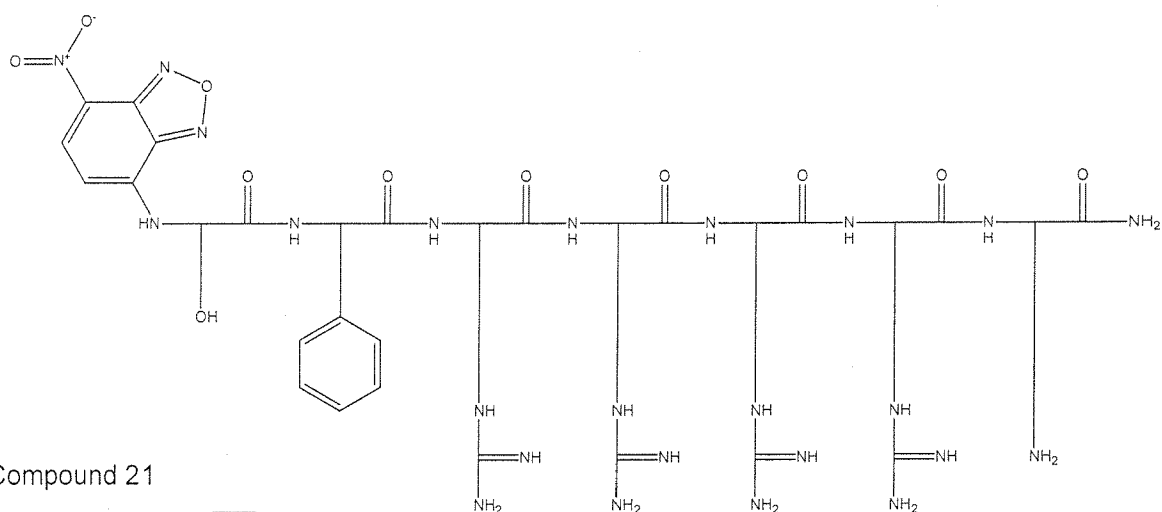


Compound 19

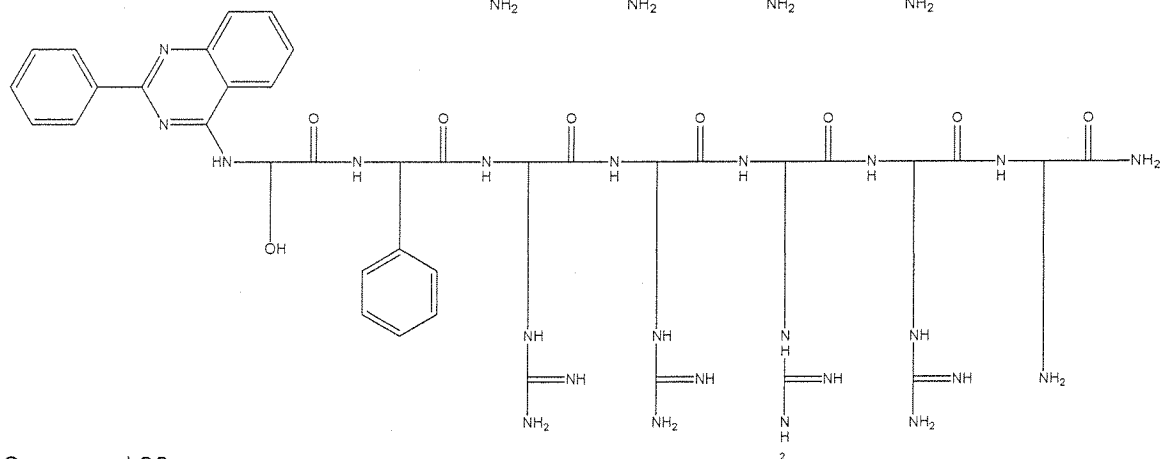
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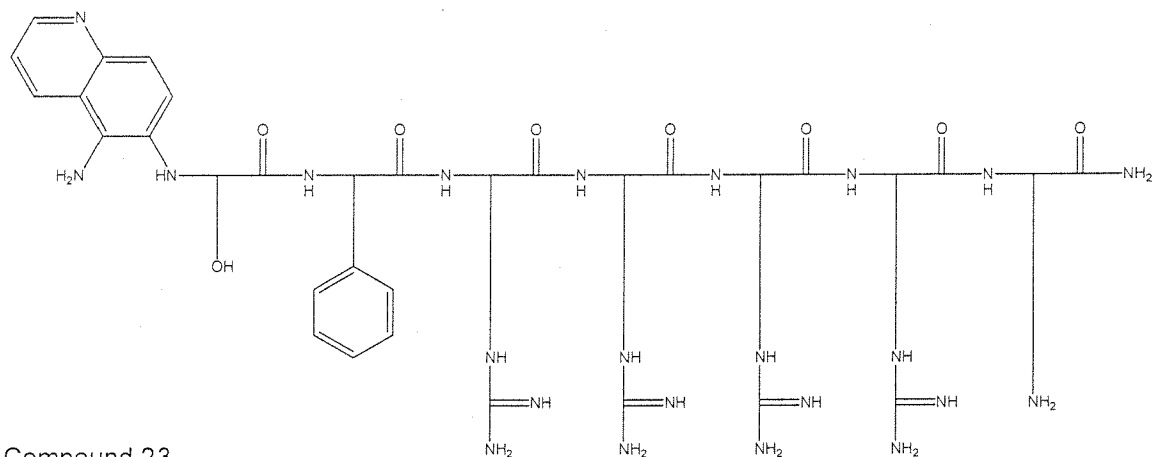
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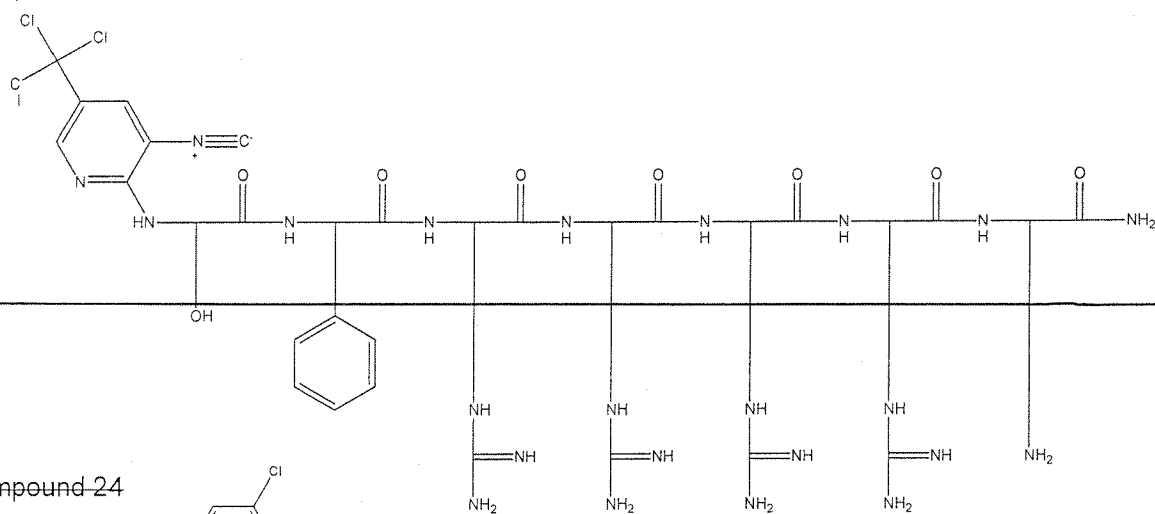
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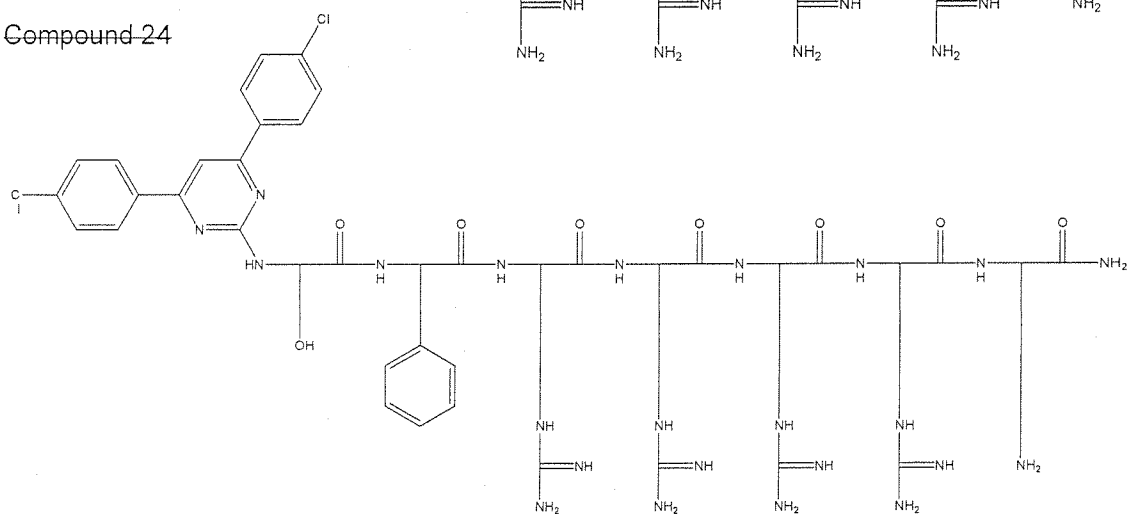
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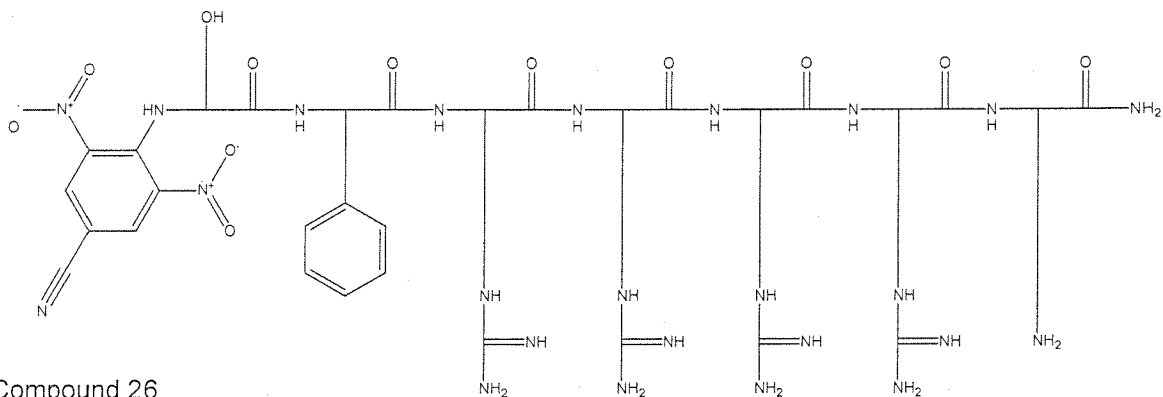
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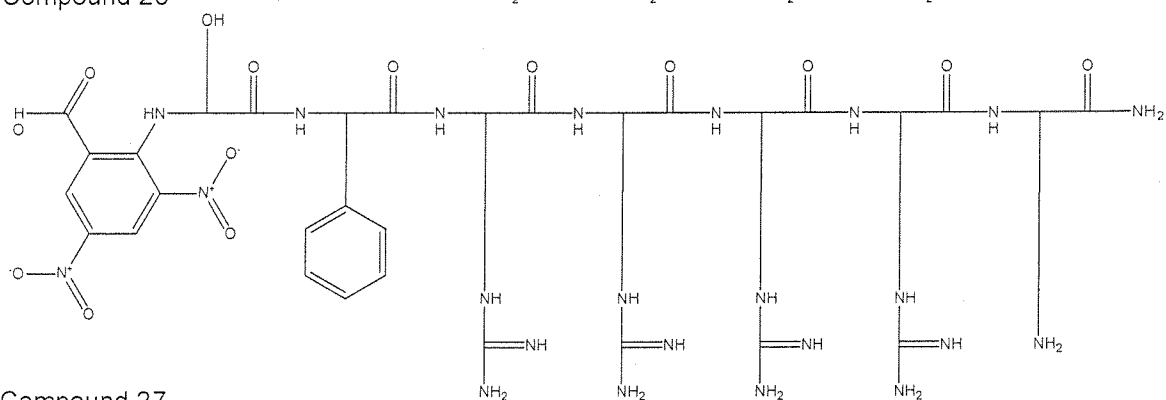
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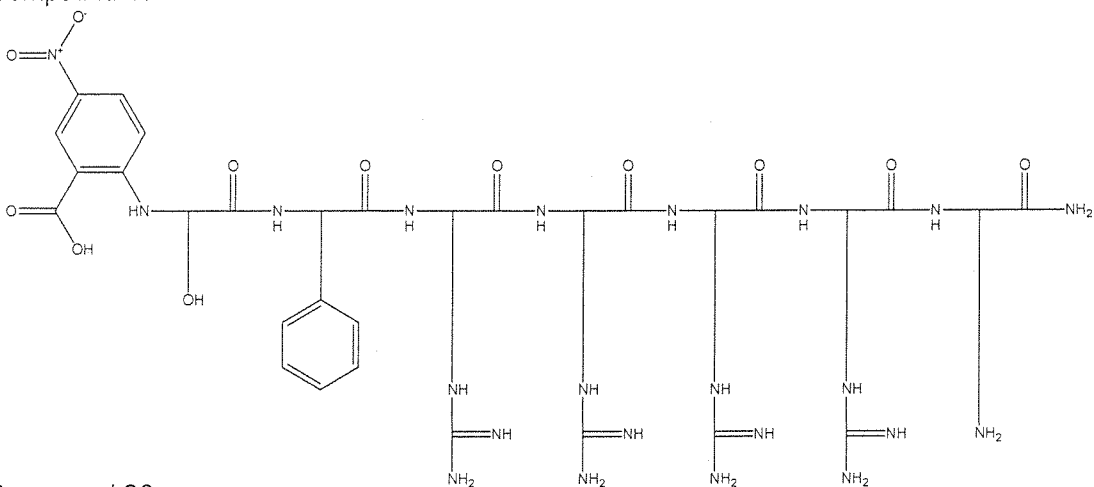
Compound 25



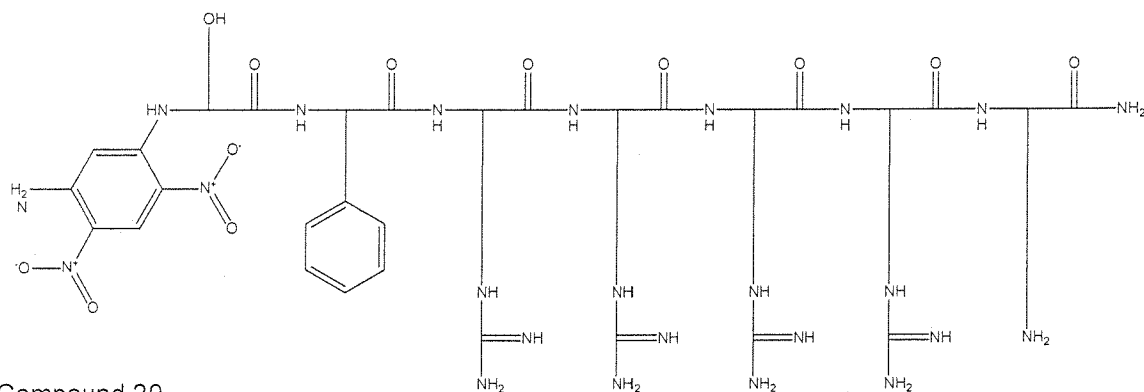
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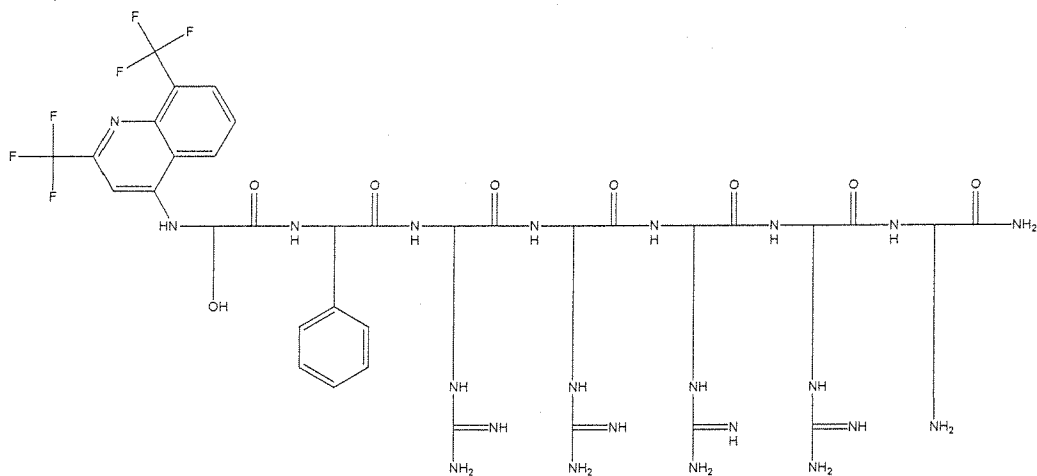
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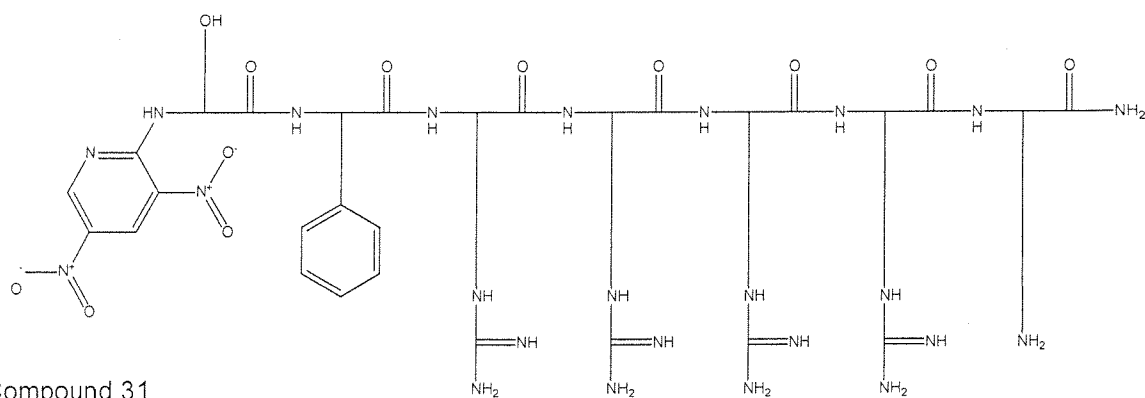
Compound 28



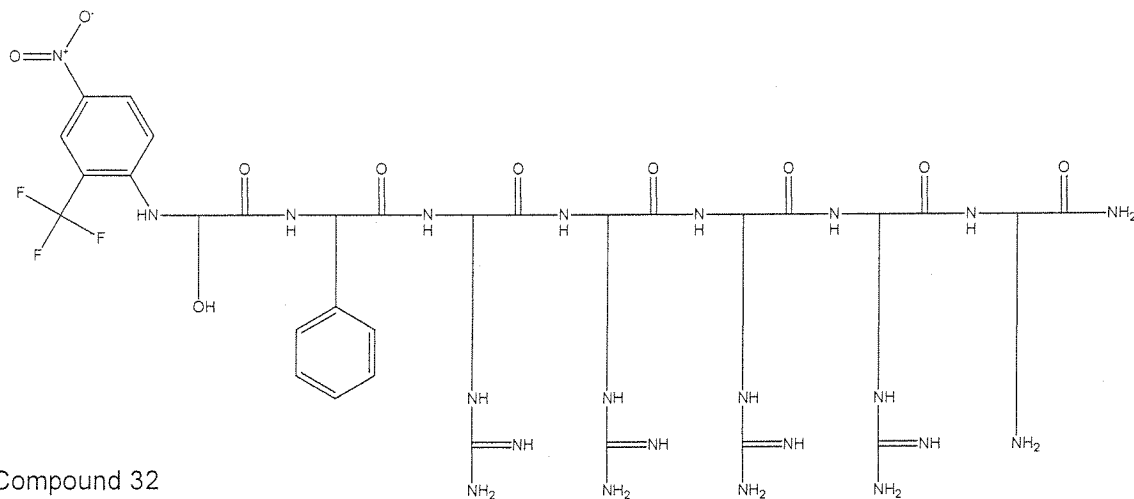
Compound 29



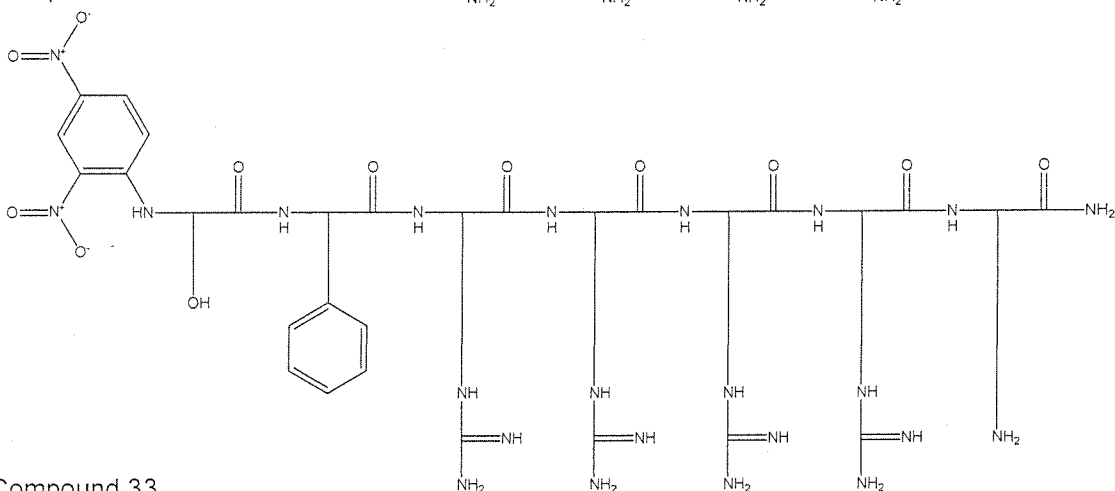
Compound 30



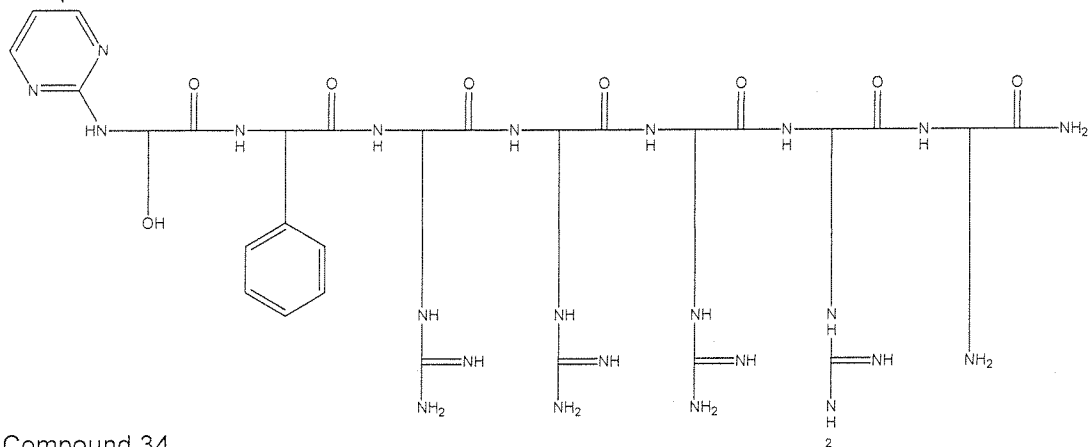
Compound 31



Compound 32

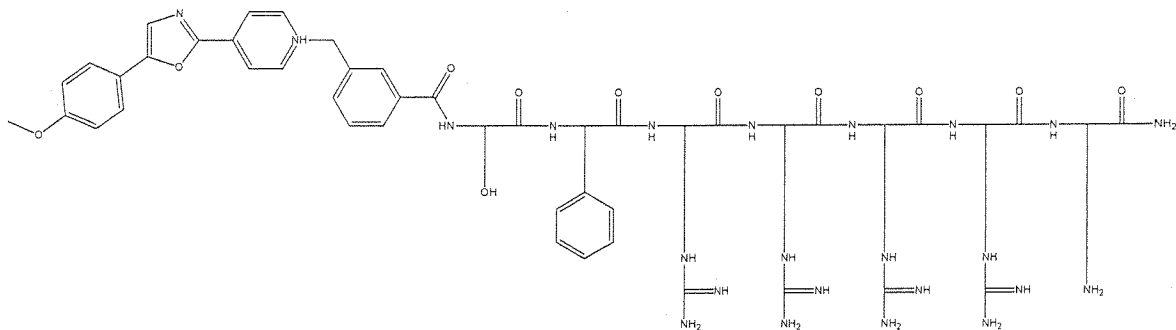


Compound 33

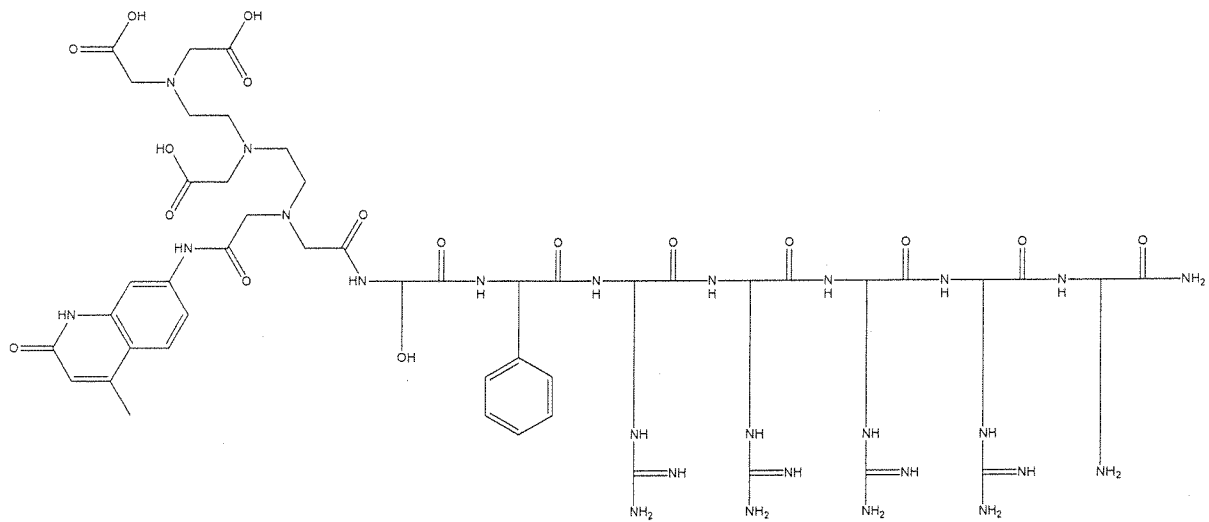


Compound 34

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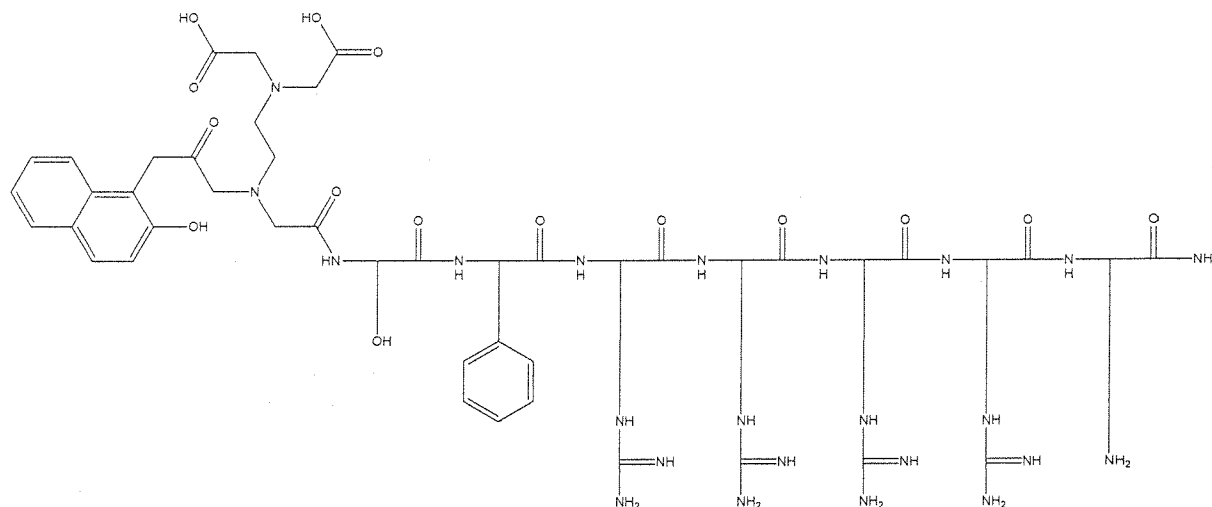


Compound 35

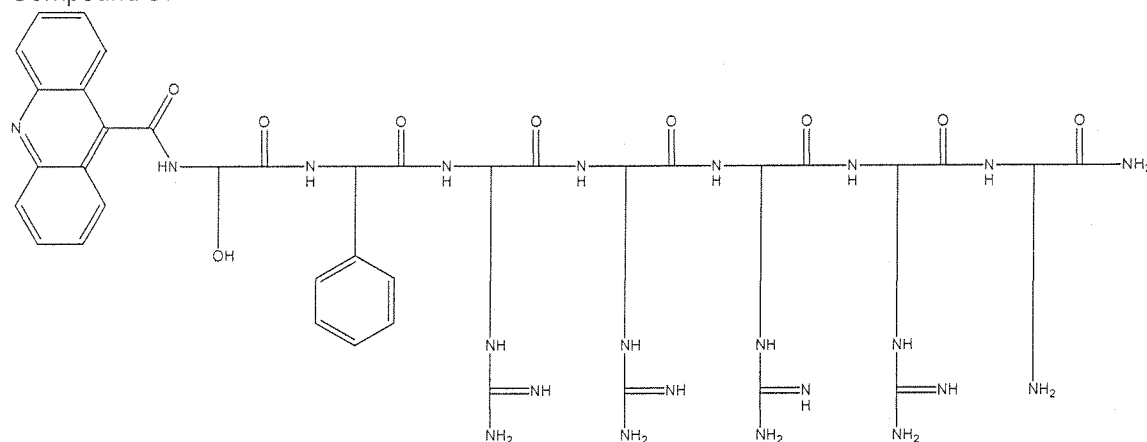


Compound 36

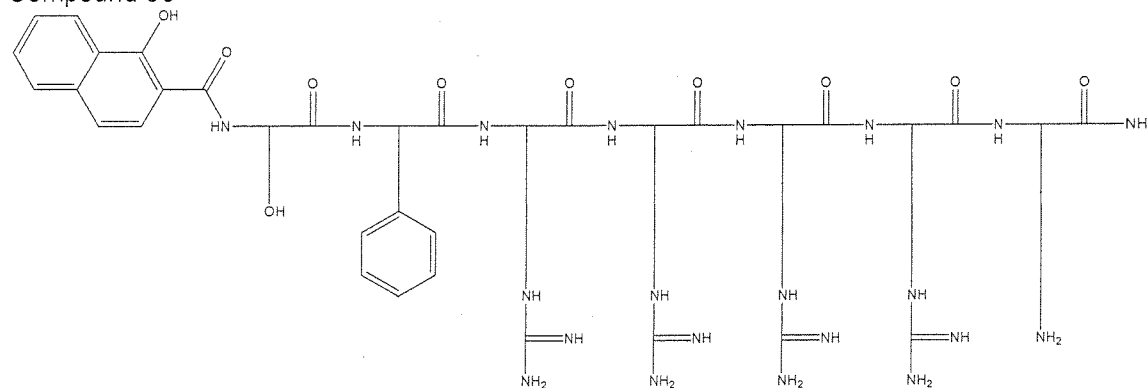
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Compound 37

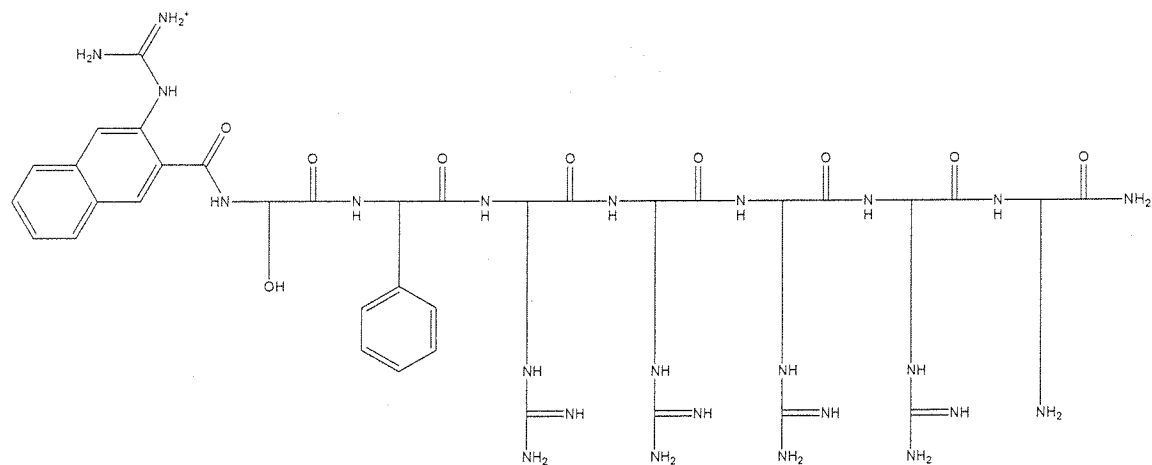


Compound 38

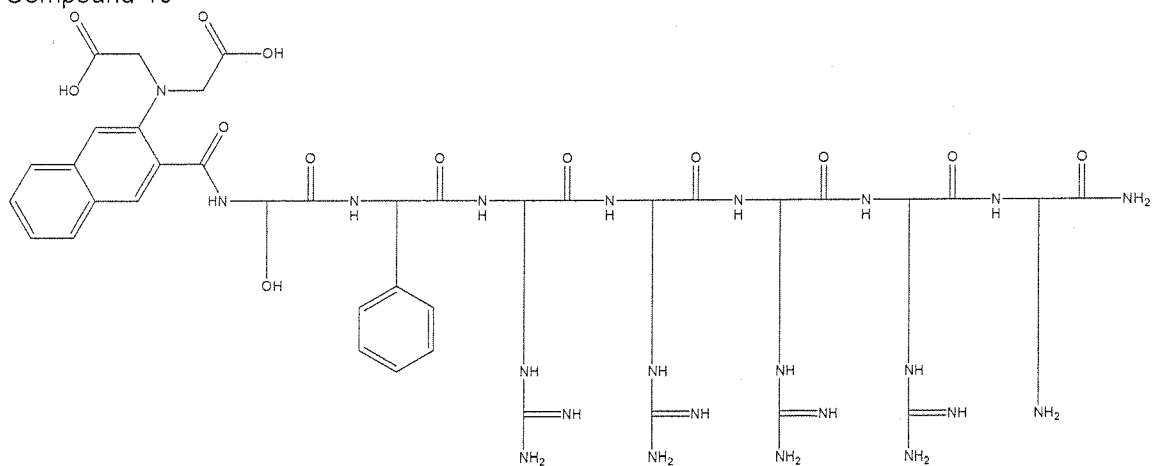


Compound 39

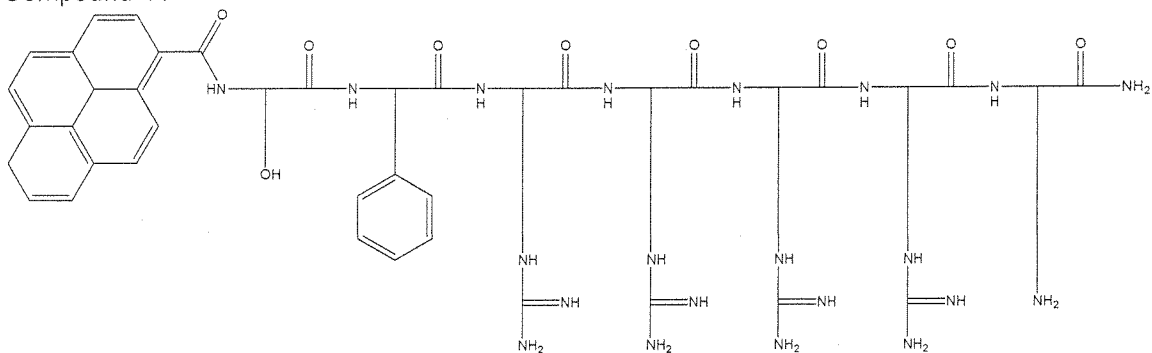
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Compound 40

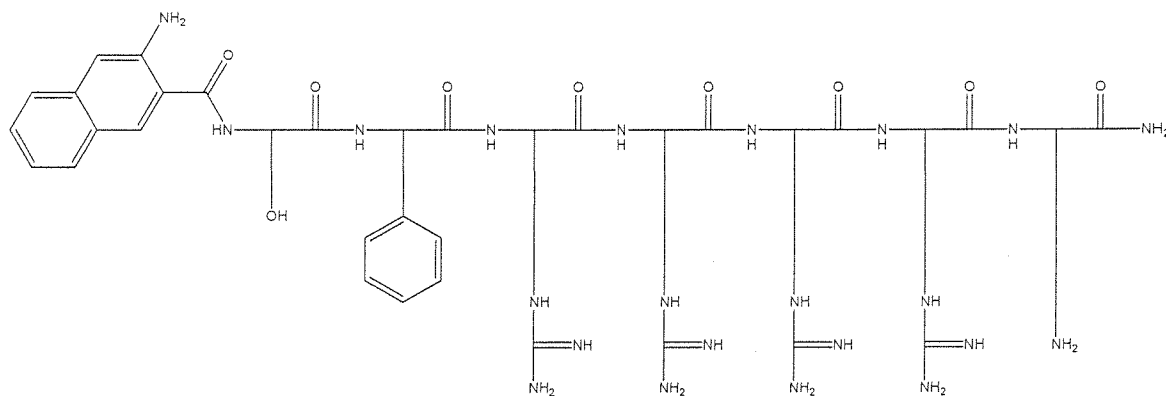


Compound 41

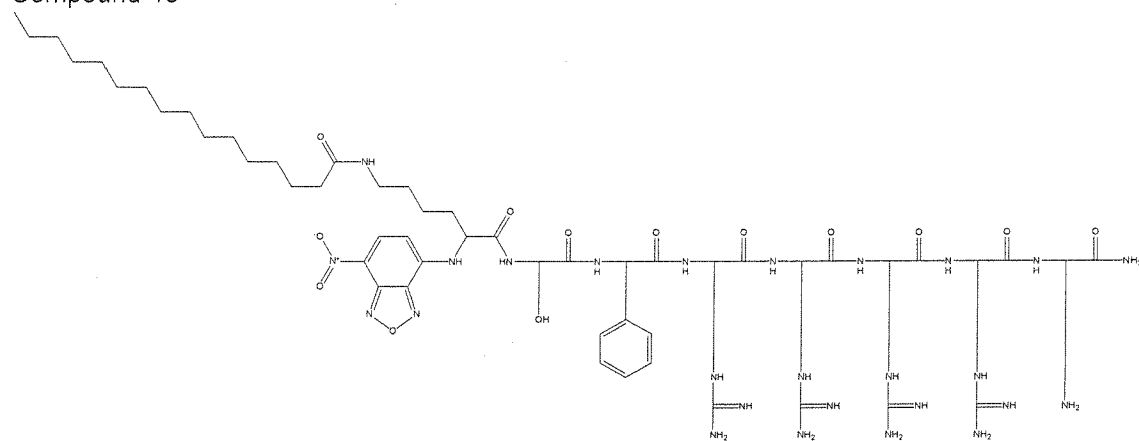


Compound 42

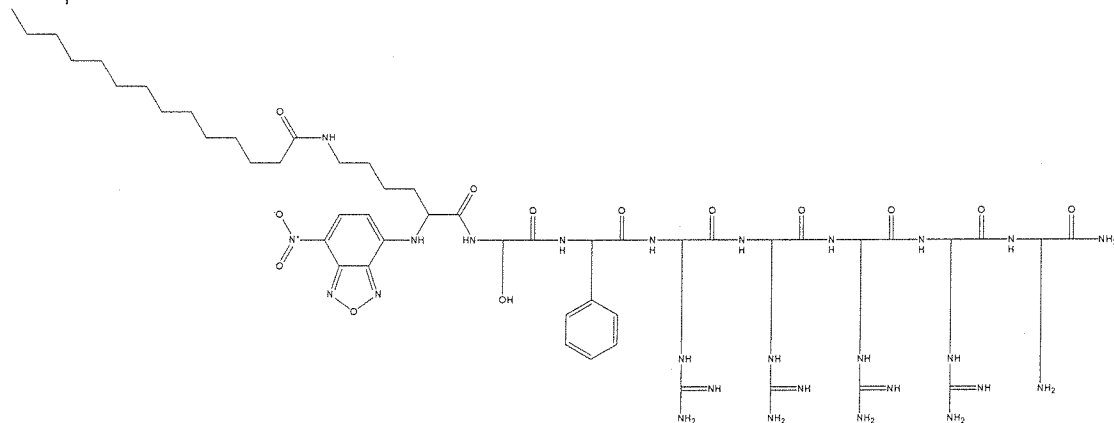
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Compound 43

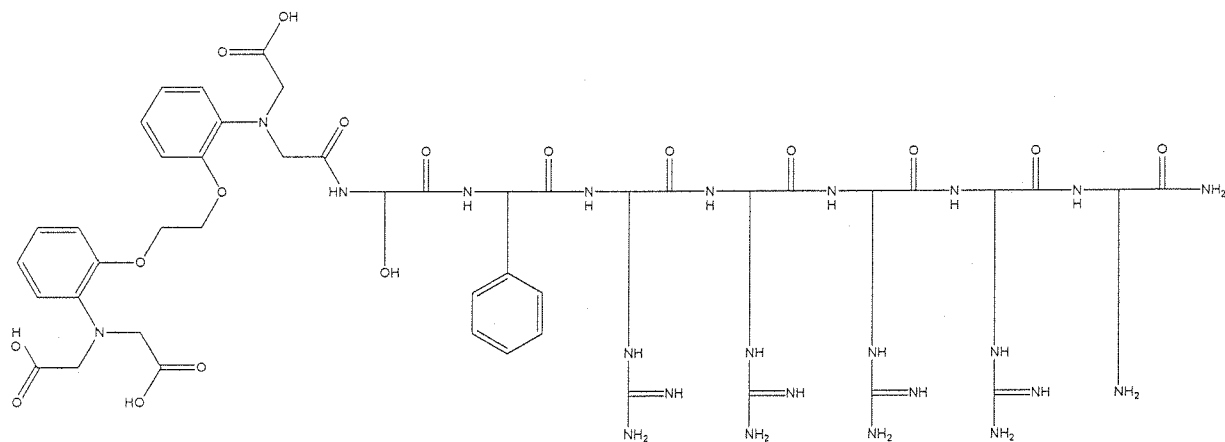


Compound 44

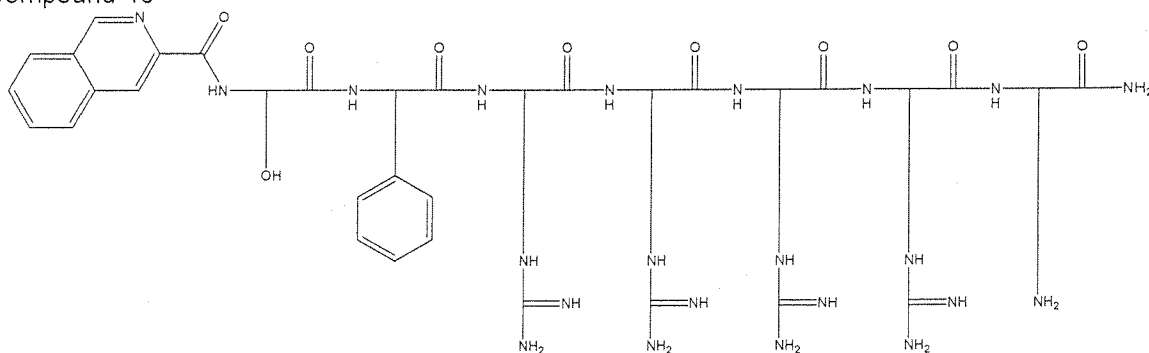


Compound 45

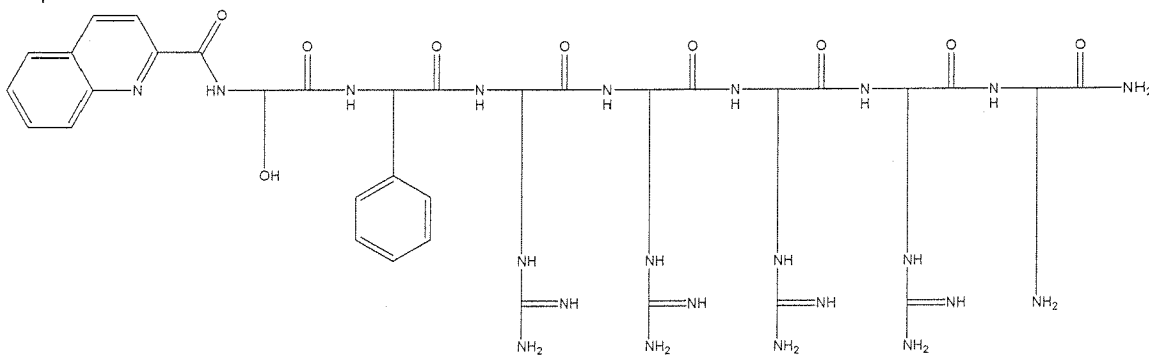
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Compound 46

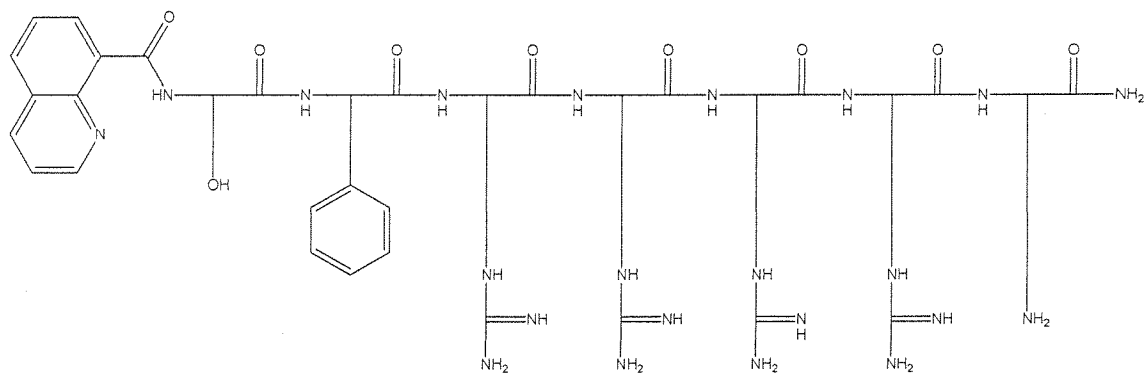


Compound 47

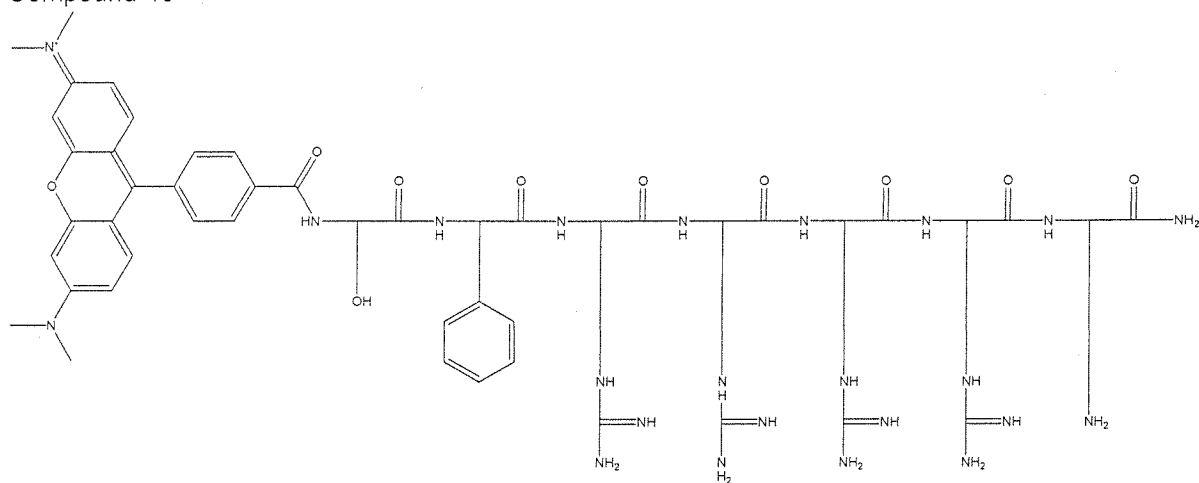


Compound 48

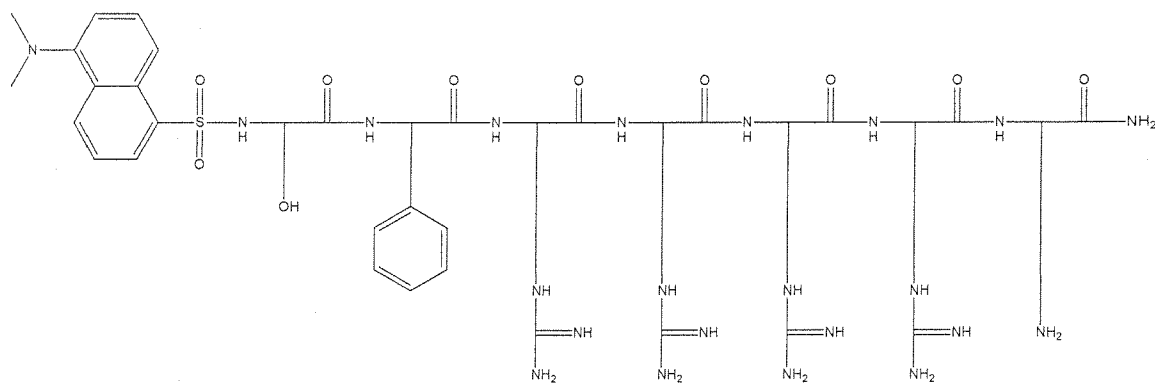
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Compound 49

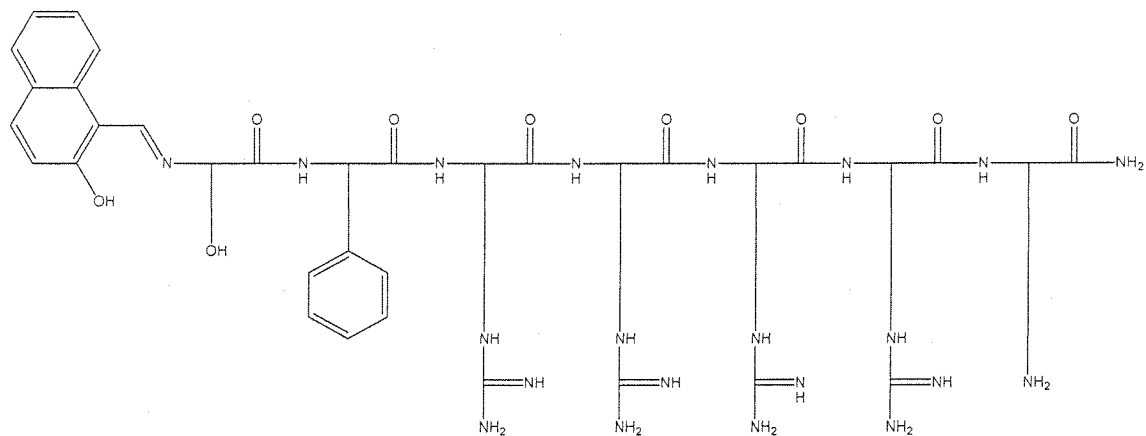


Compound 50

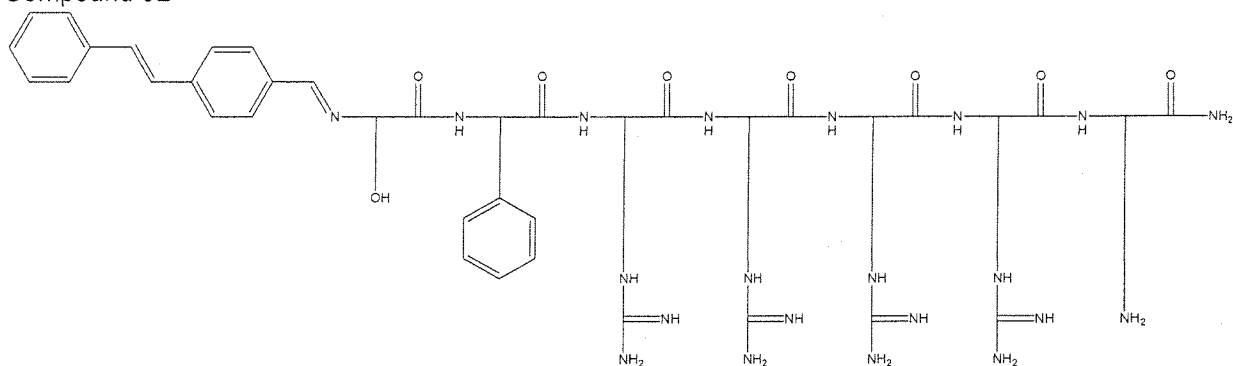


Compound 51

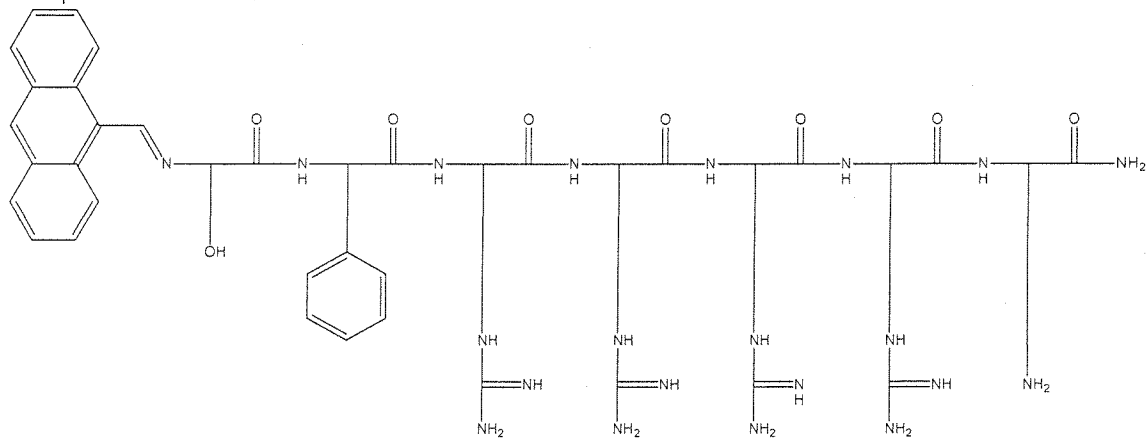
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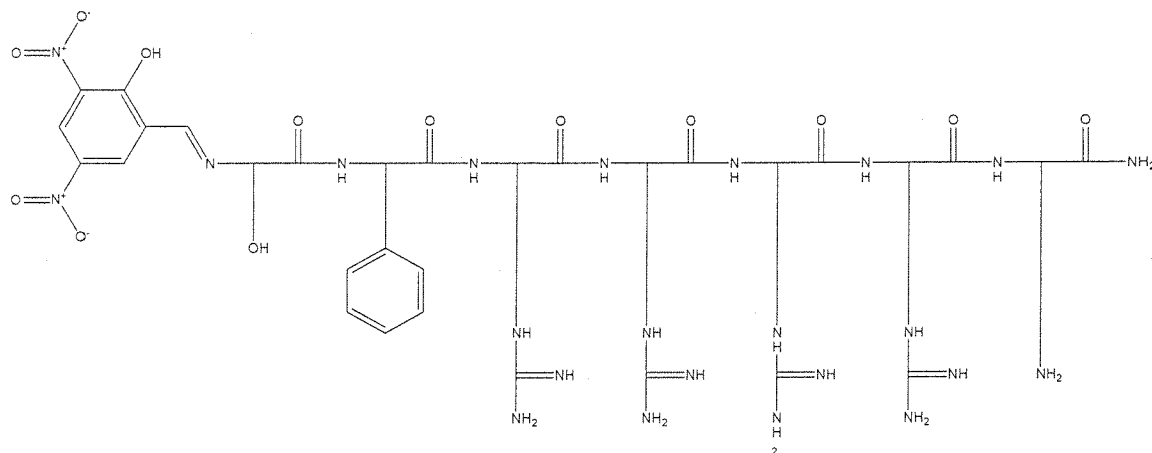
Compound 52



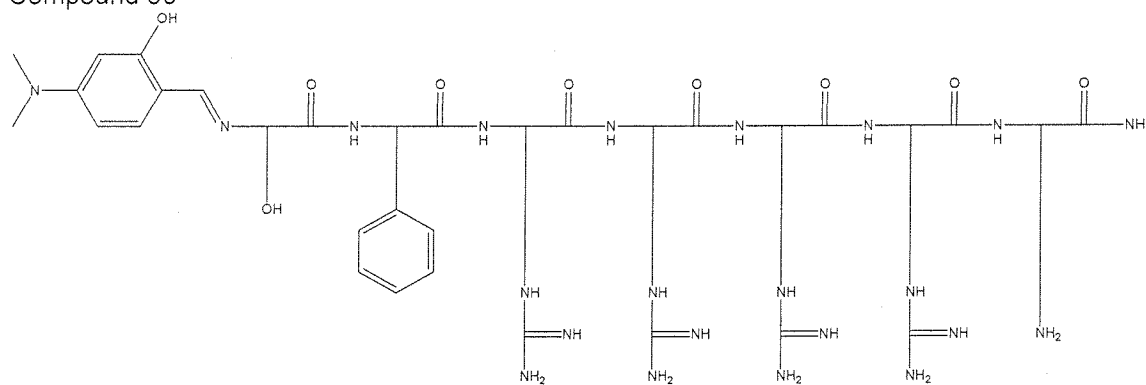
Compound 53



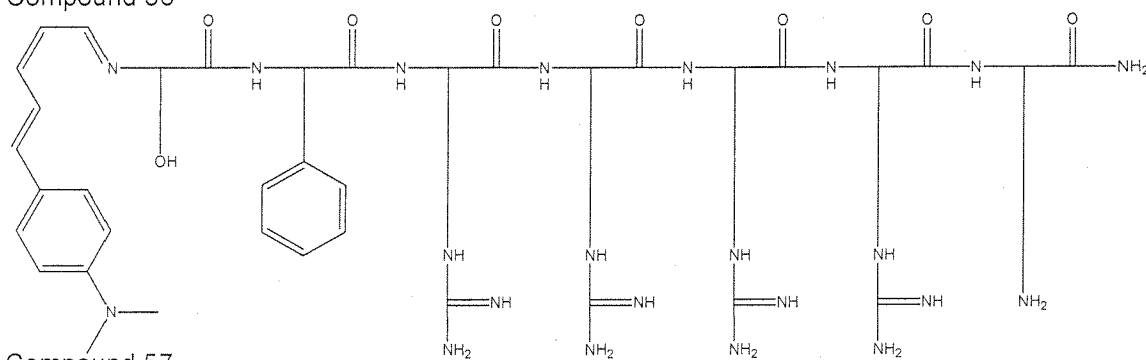
Compound 54



Compound 55

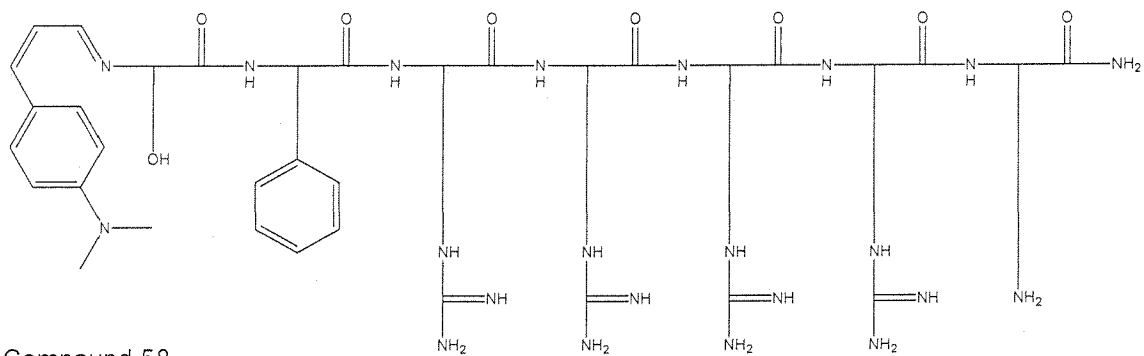


Compound 56

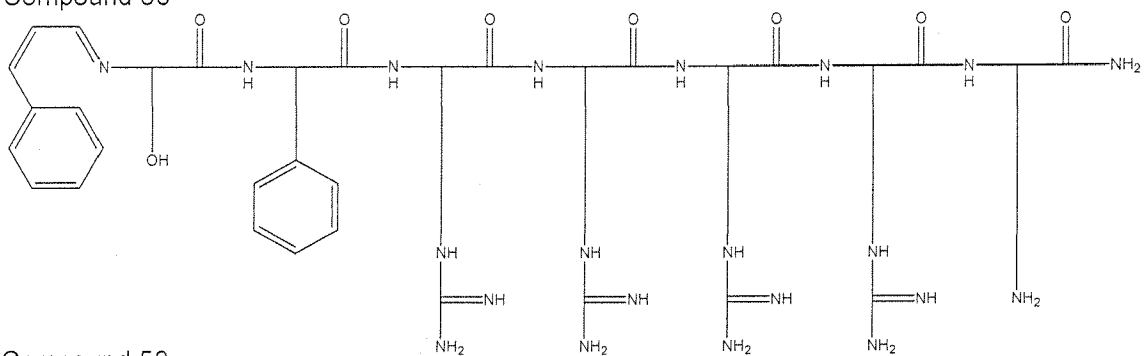


Compound 57

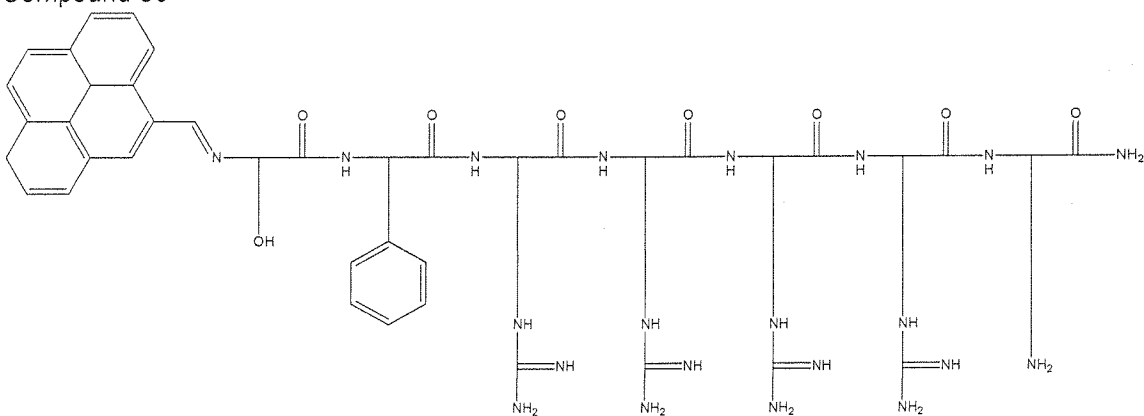
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Compound 58

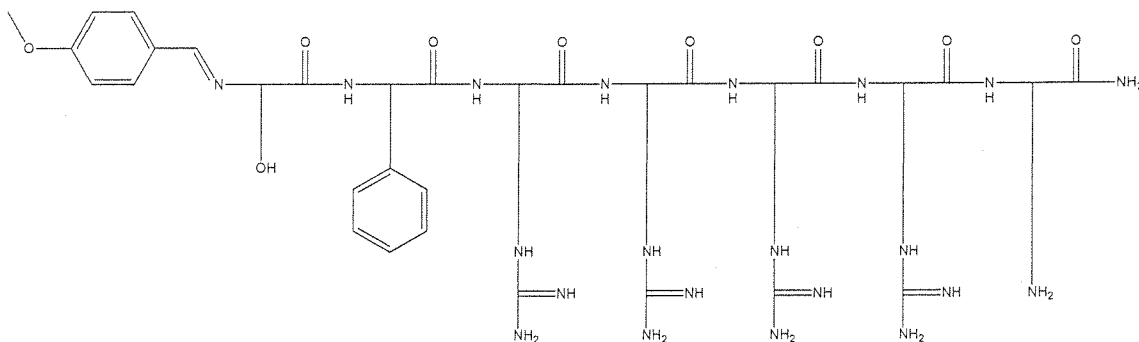


Compound 59

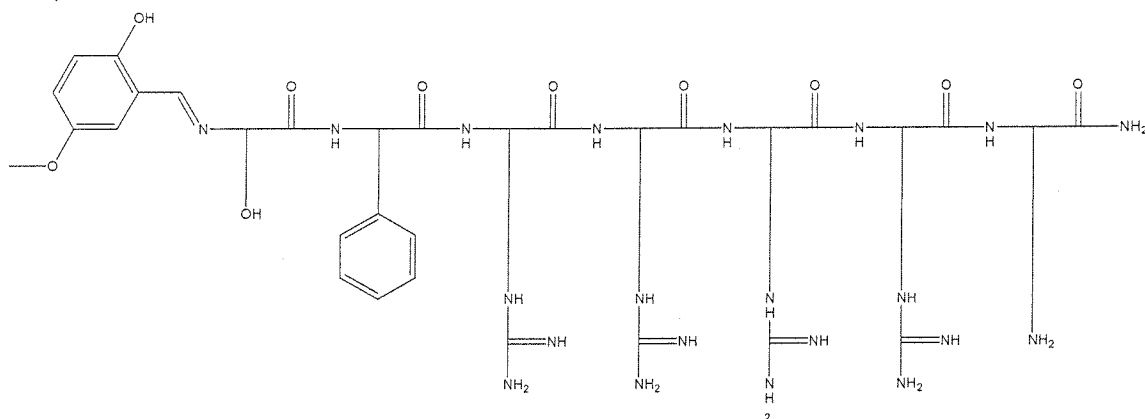


Compound 60

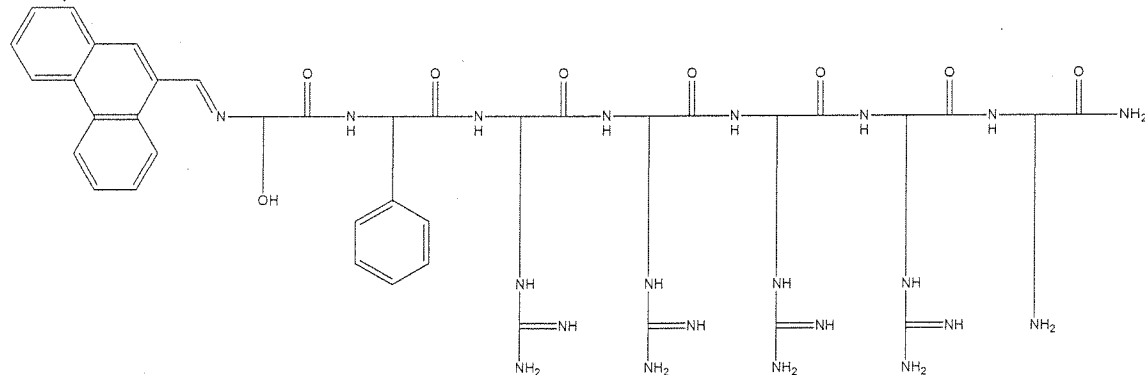
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Compound 61

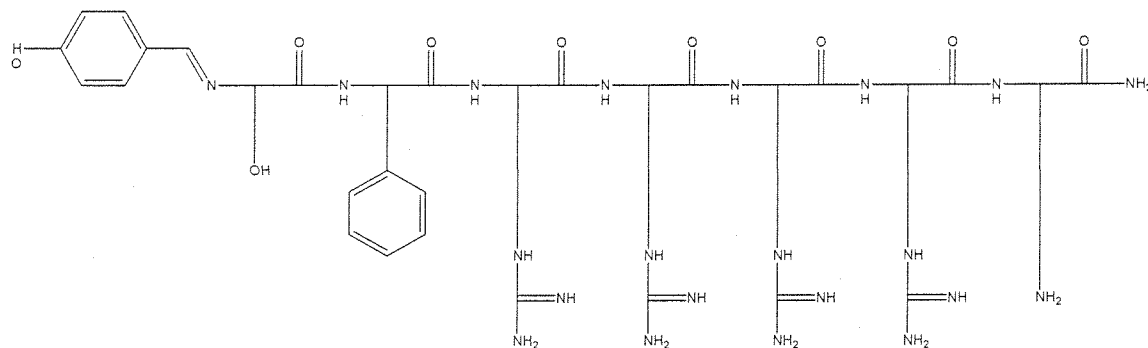


Compound 62

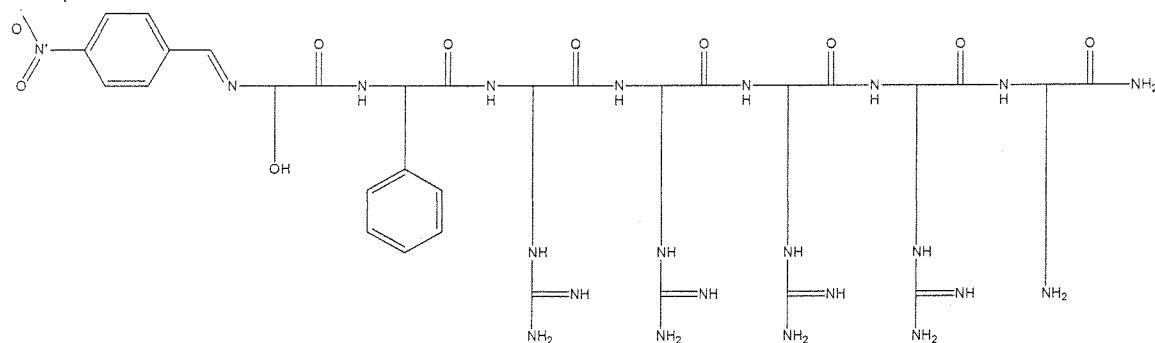


Compound 63

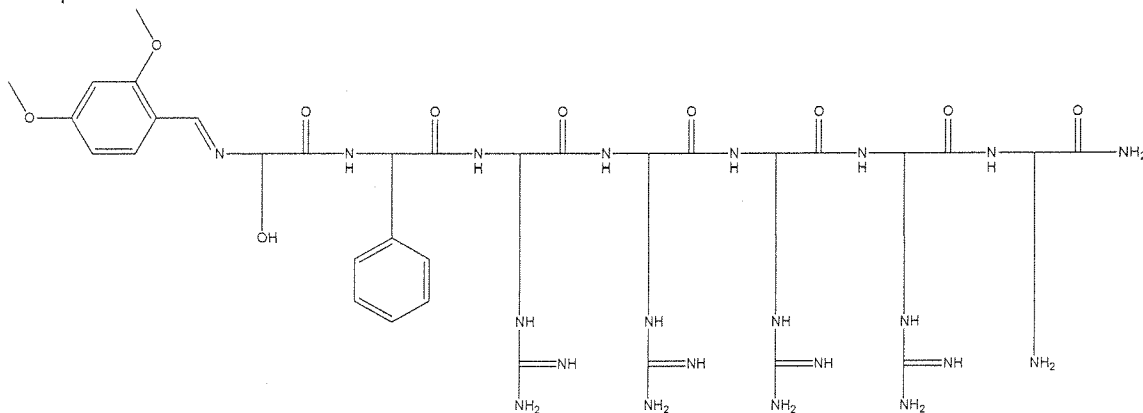
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Compound 64

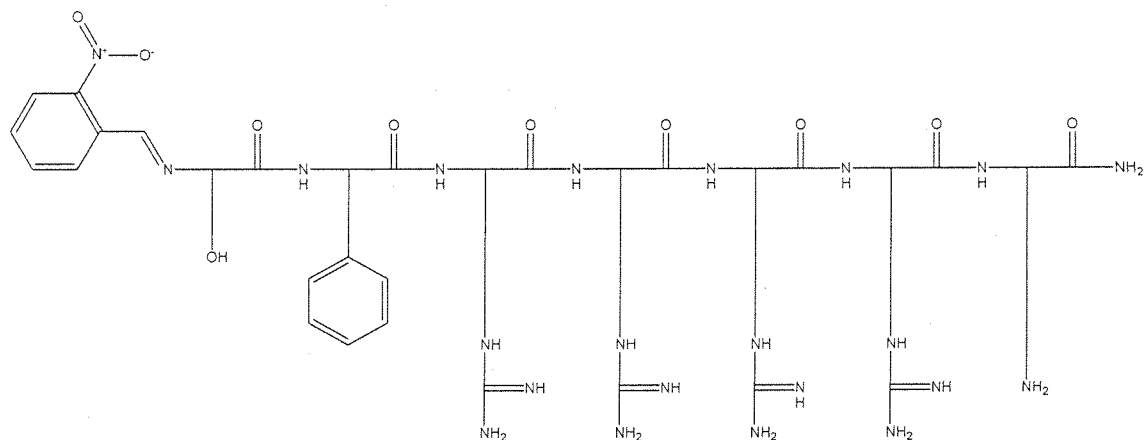


Compound 65

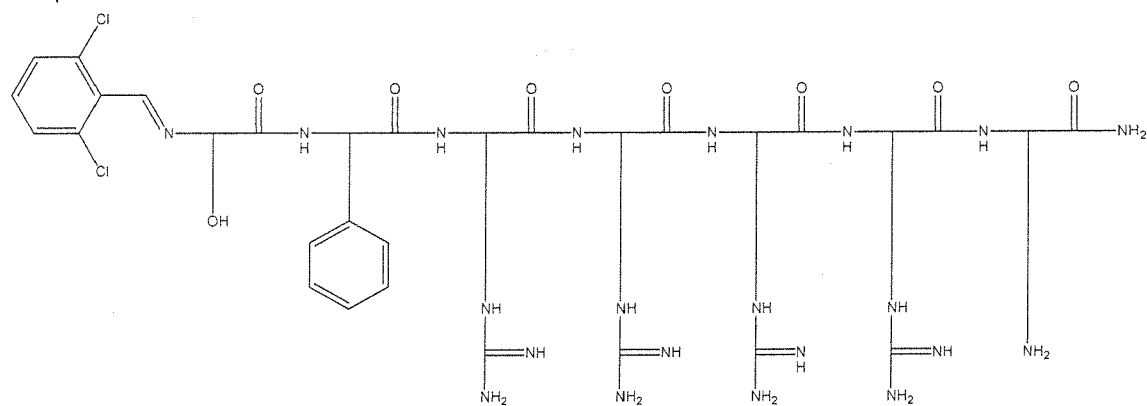


Compound 66

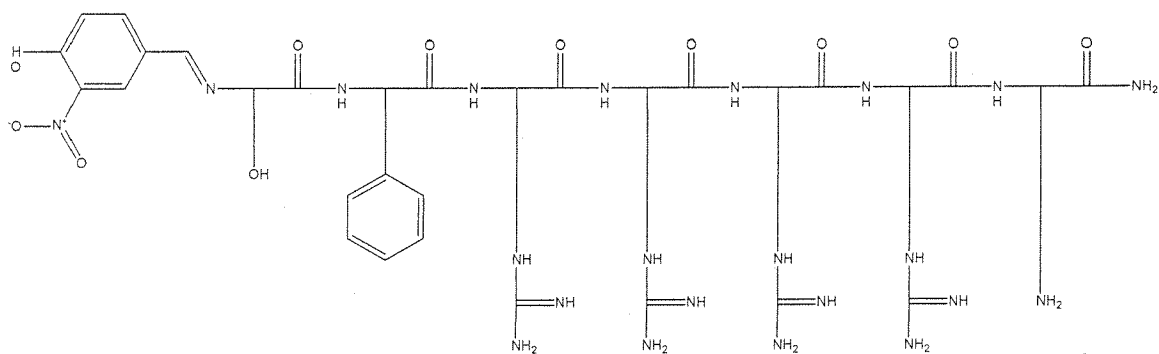
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Compound 67

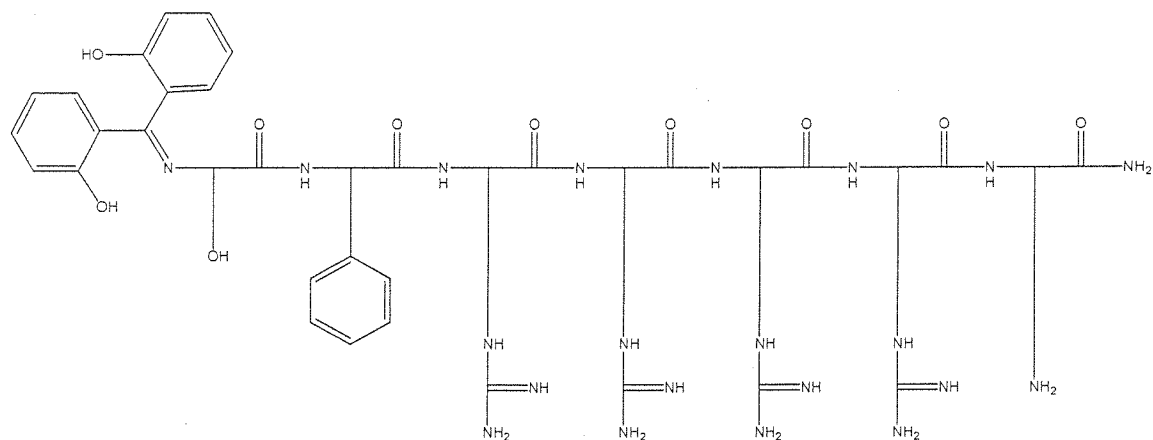


Compound 68

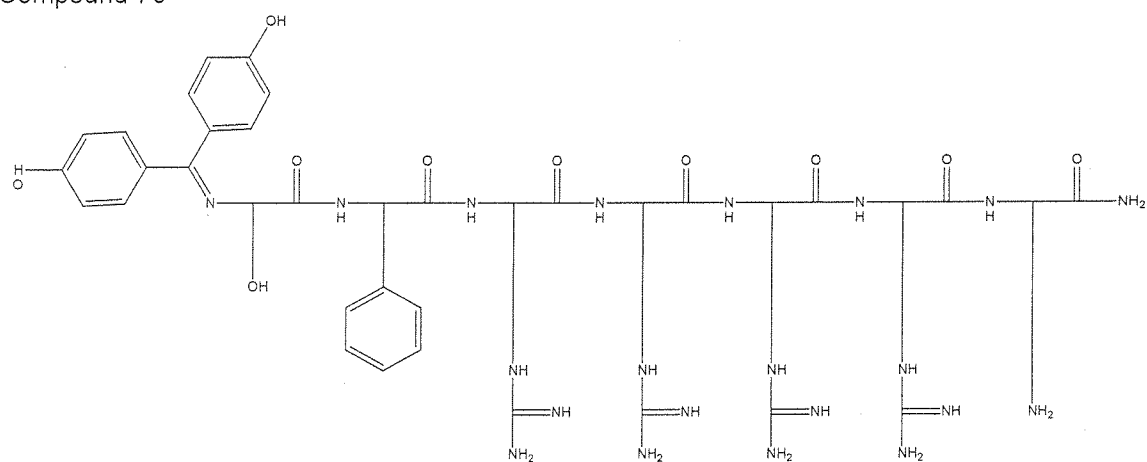


Compound 69

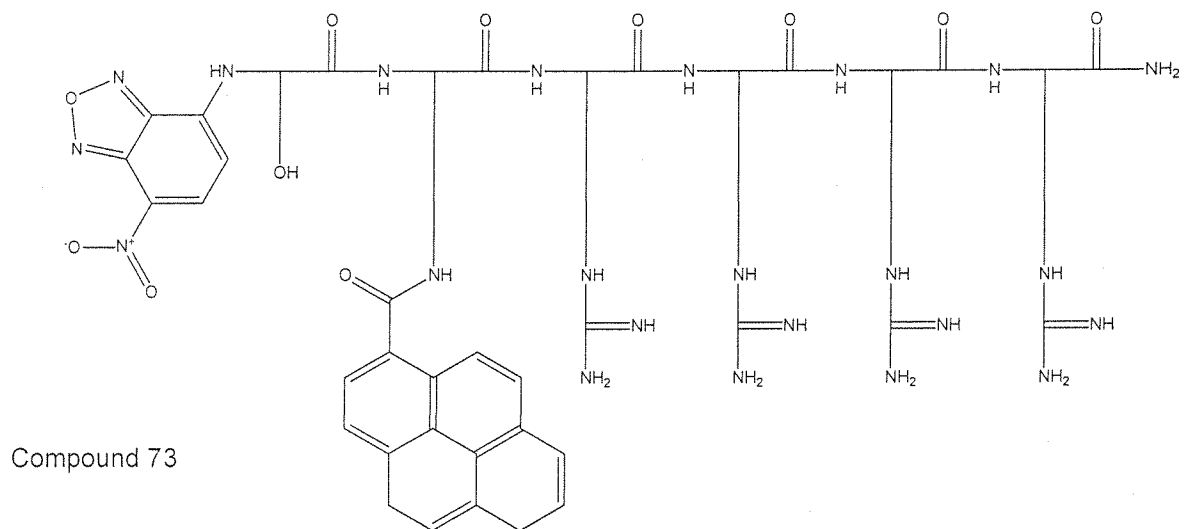
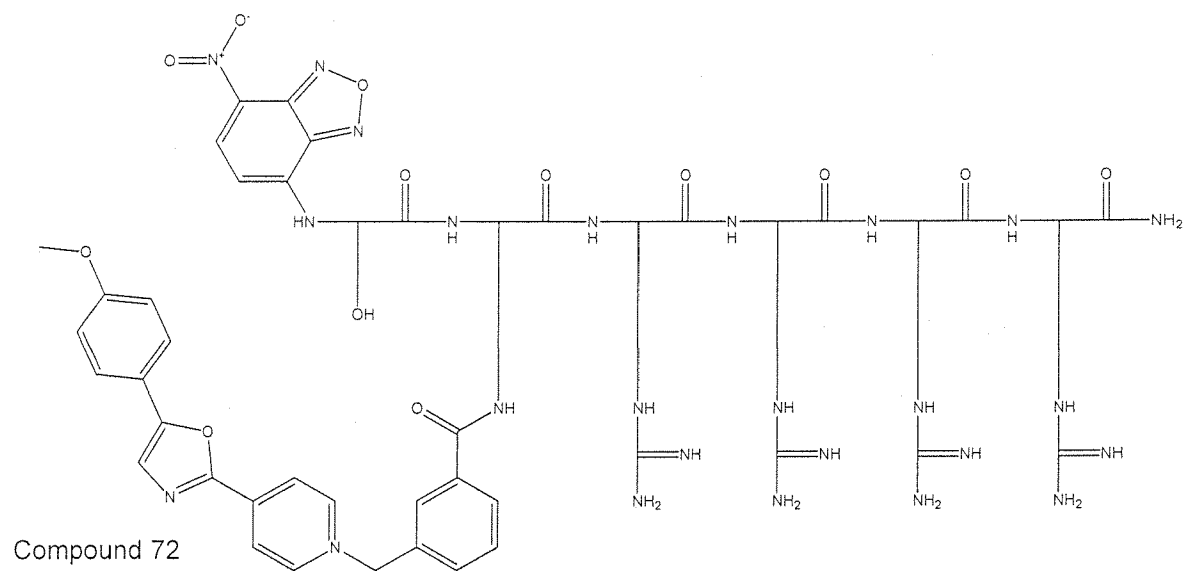
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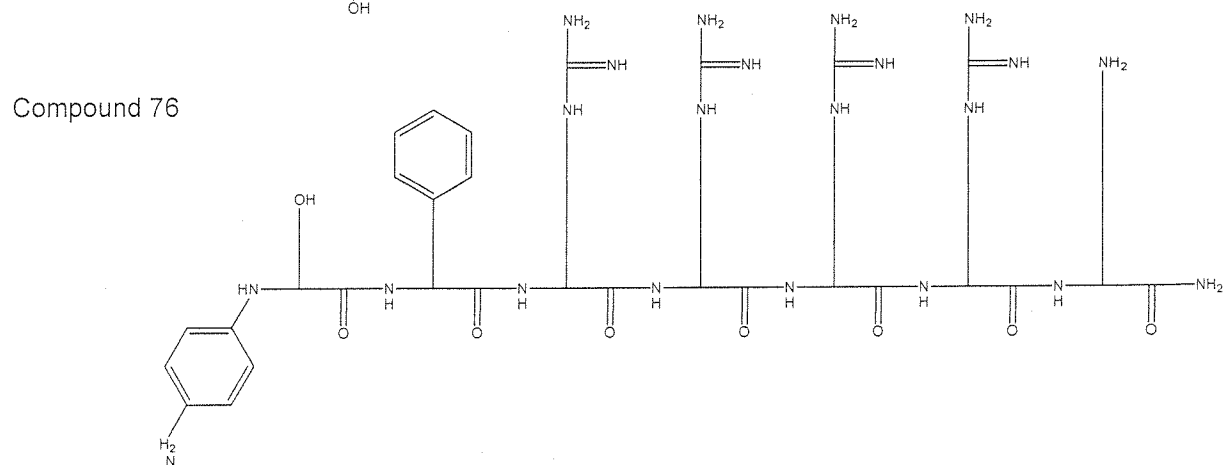
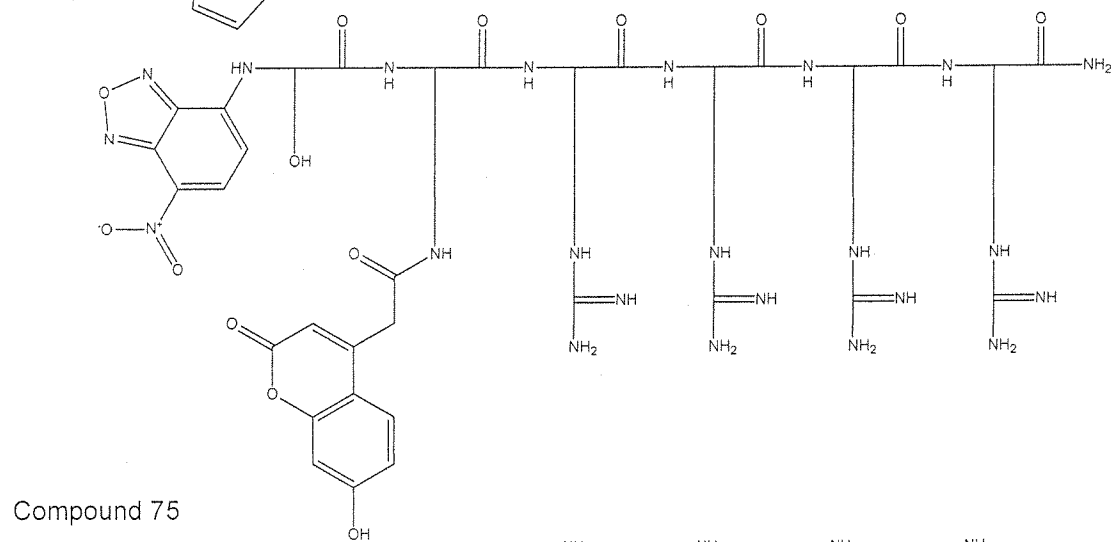
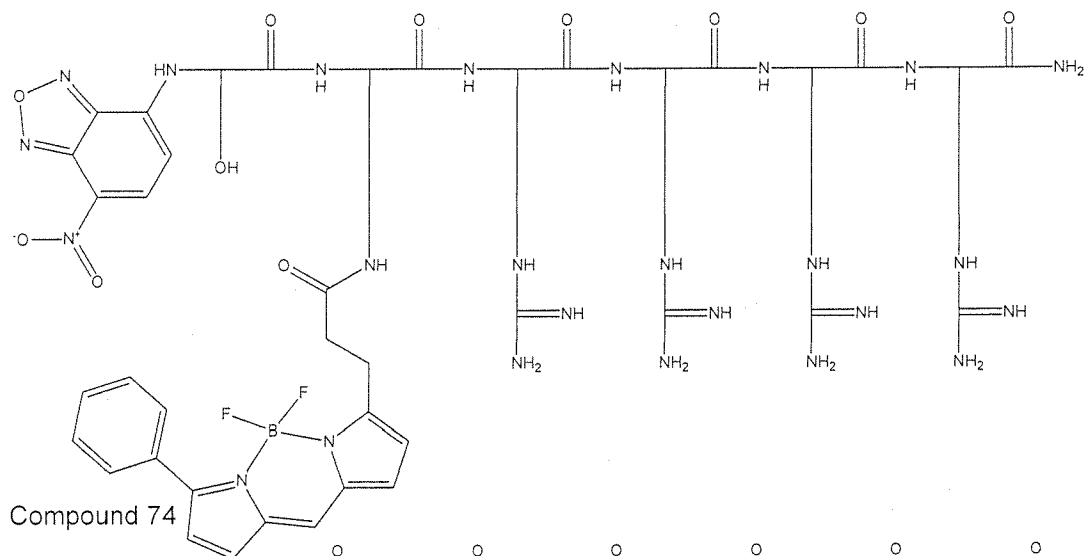


Compound 70

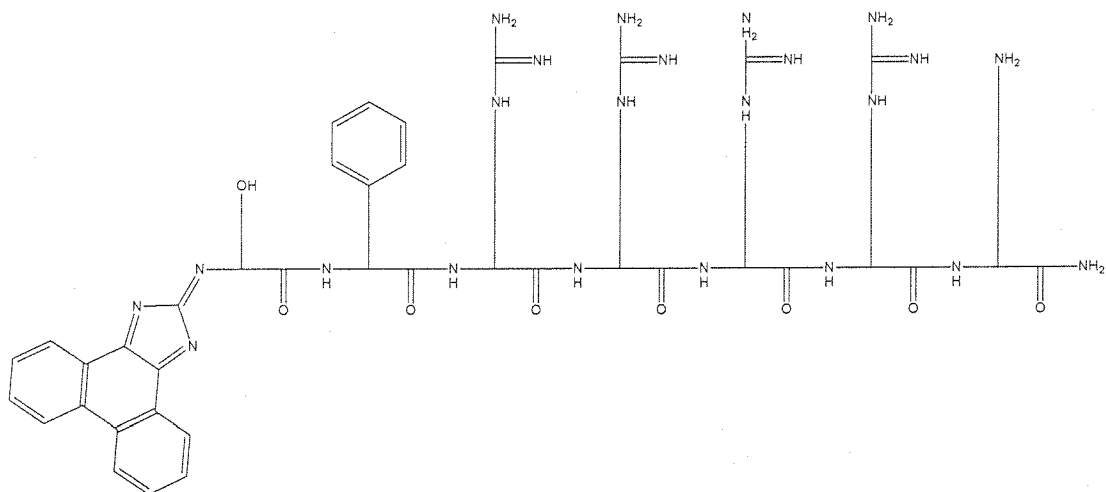


Compound 71

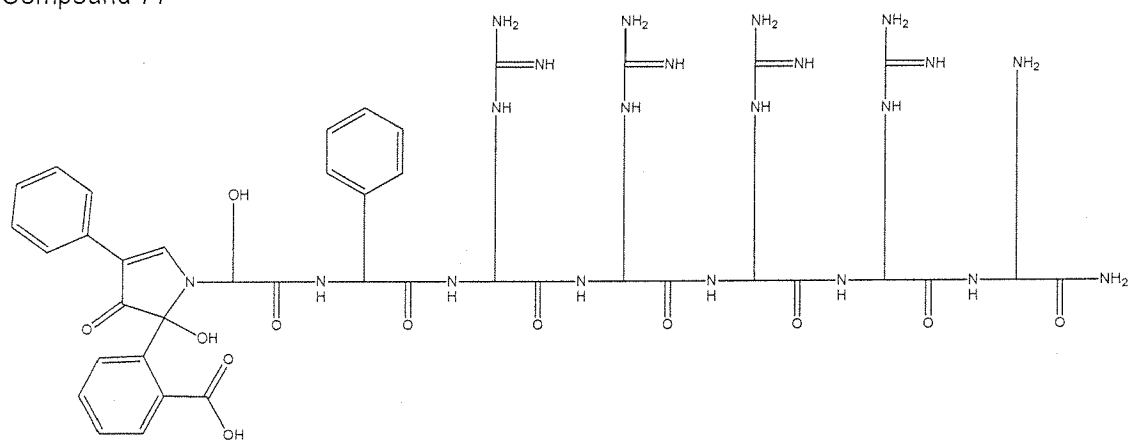




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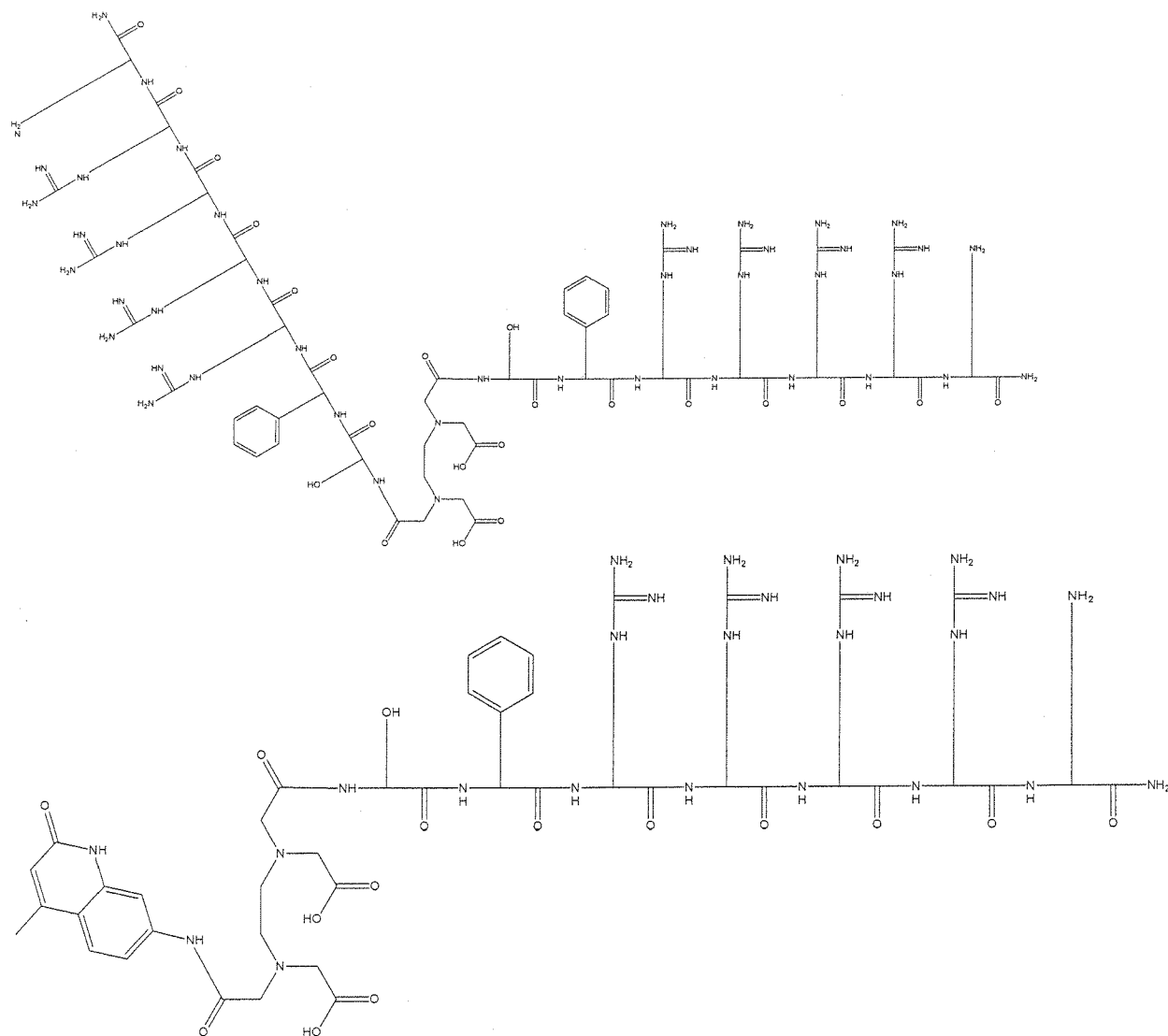
Compound 77



Compound 78

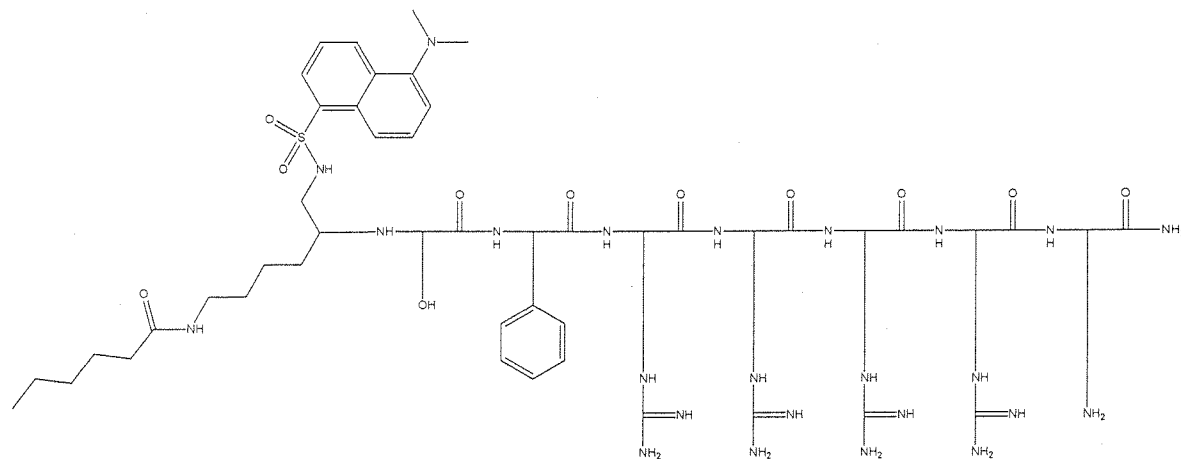
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Compound 79



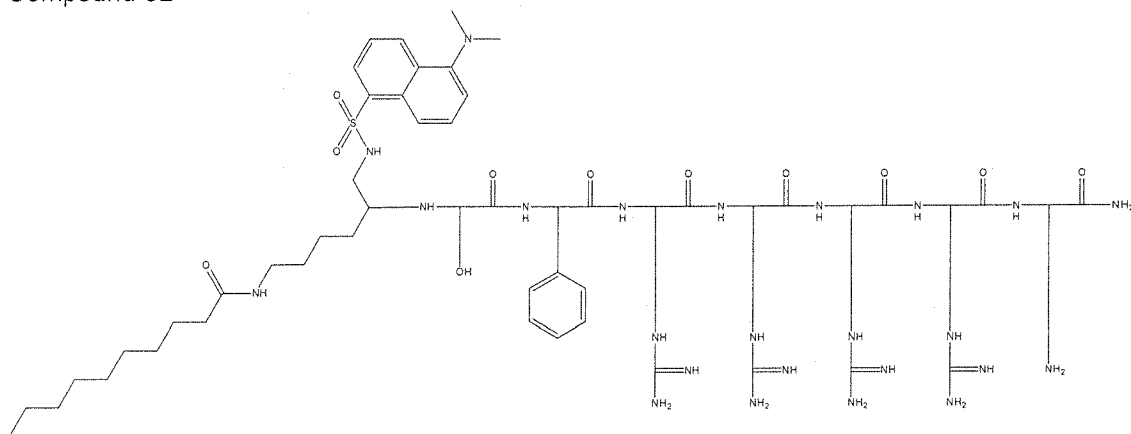
Compound 80

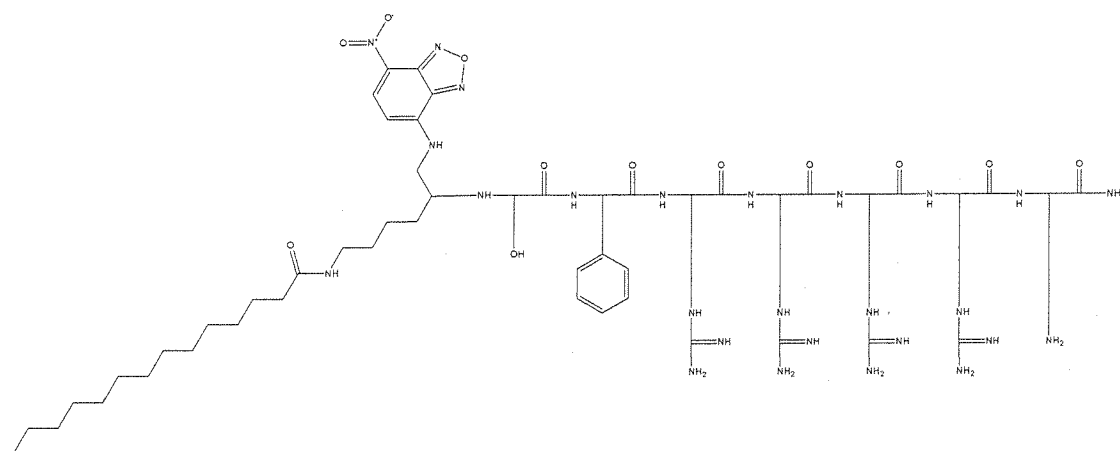
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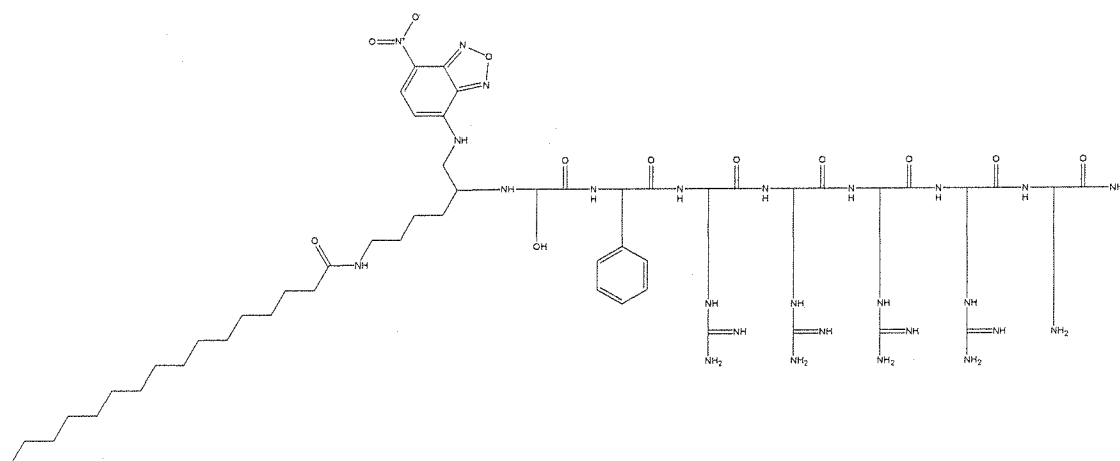
Compound 81

Compound 82

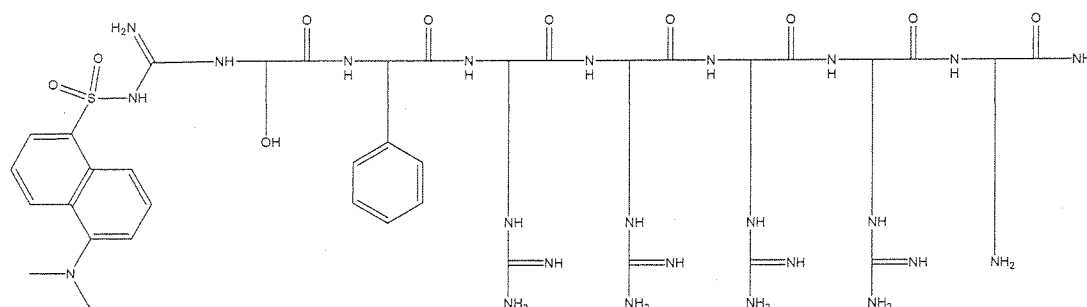




Compound 83

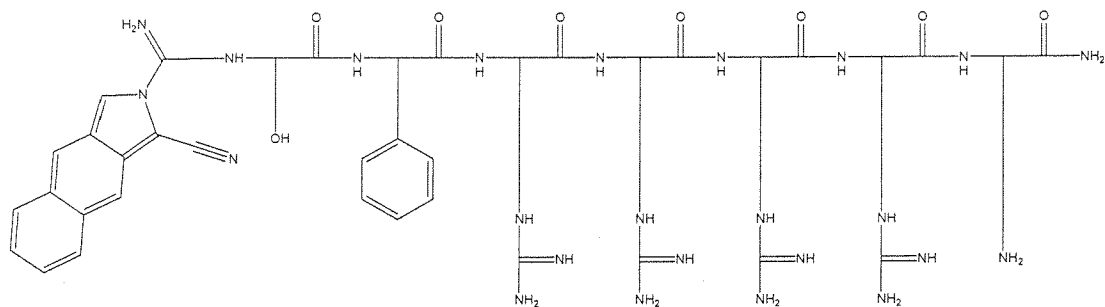


Compound 84

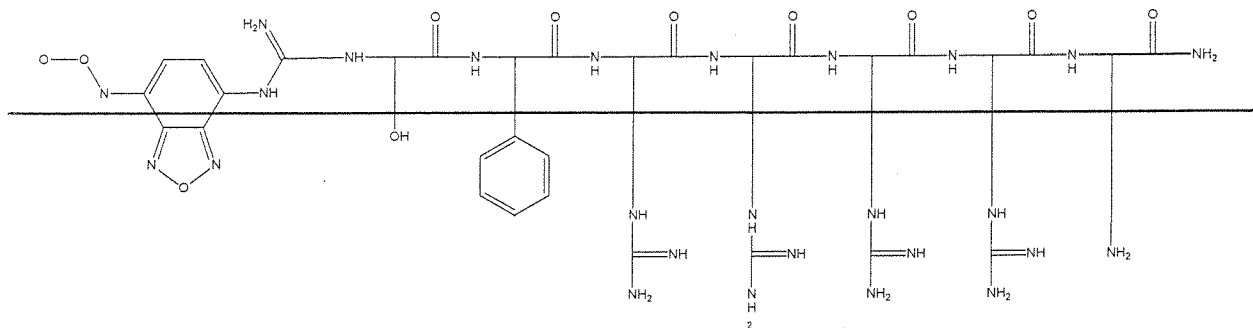


Compound 85

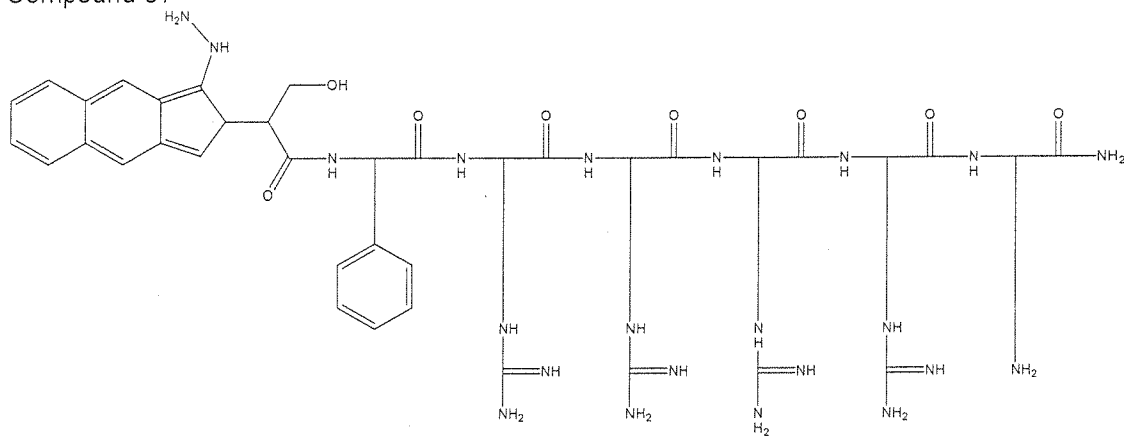
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Compound 86

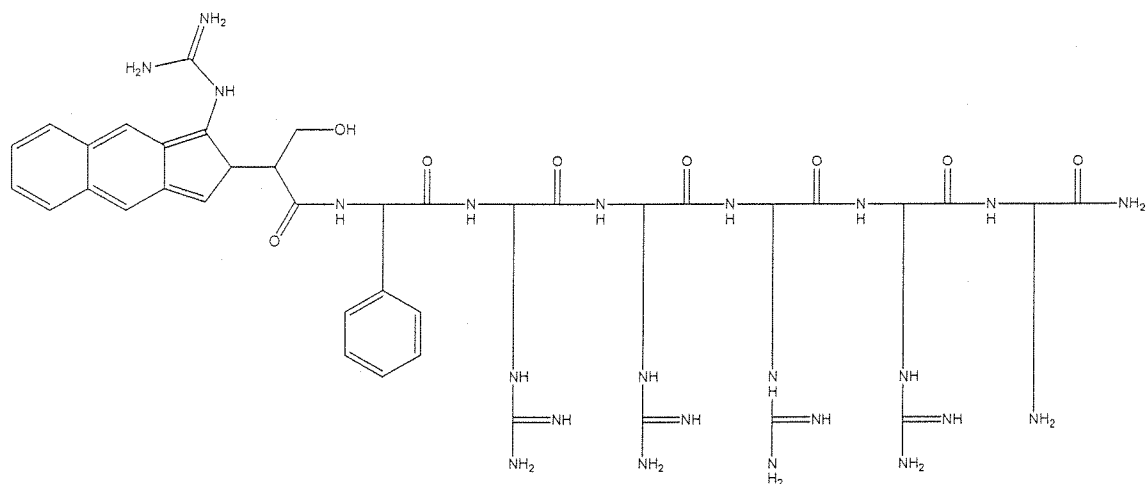


Compound 87

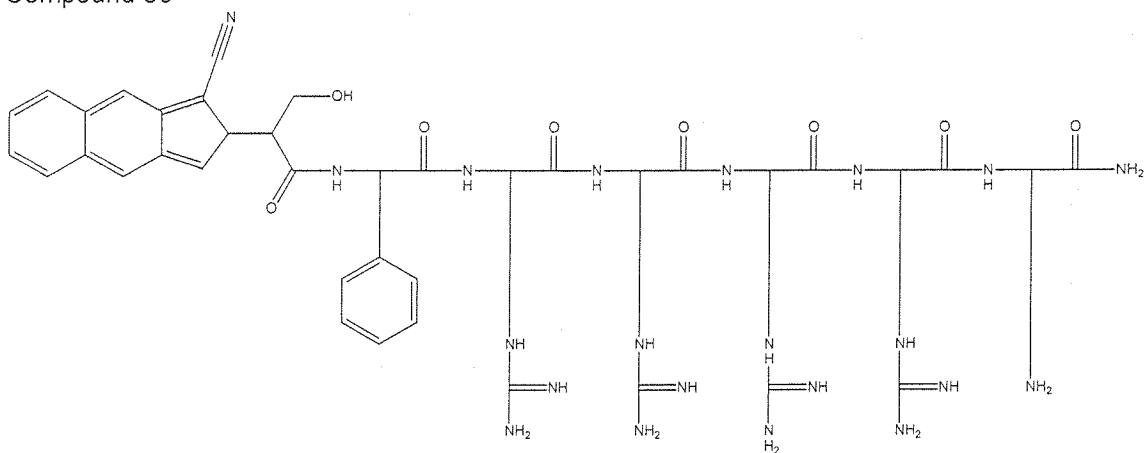


Compound 88

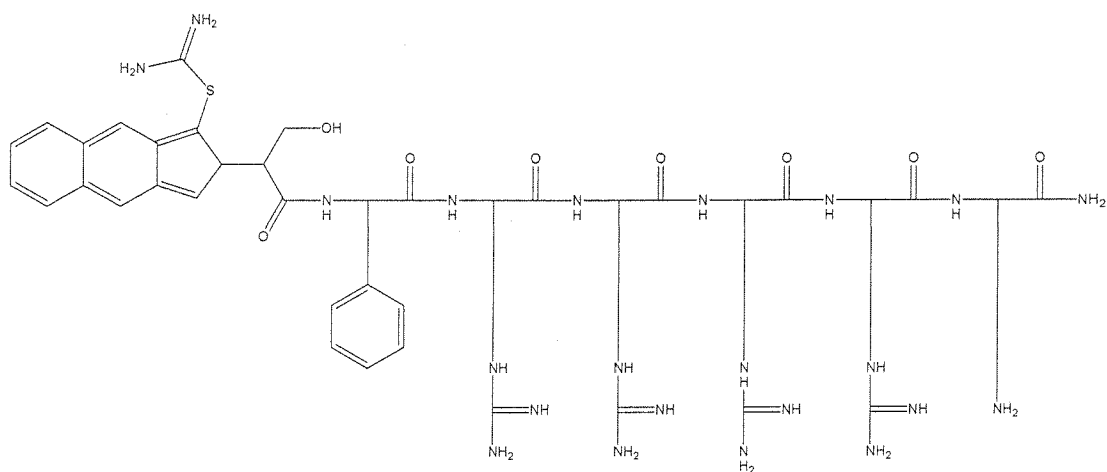
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Compound 89

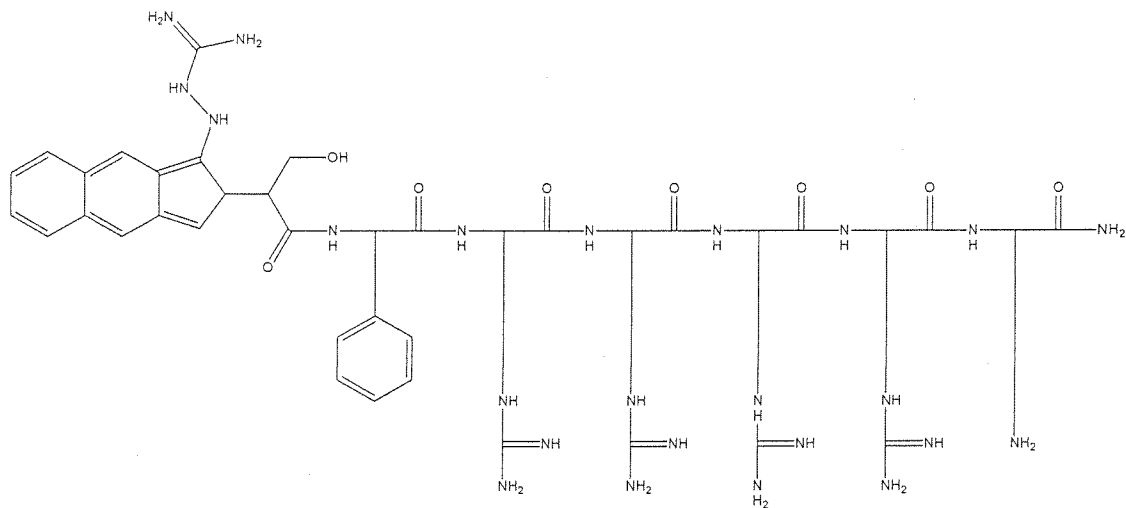


Compound 90

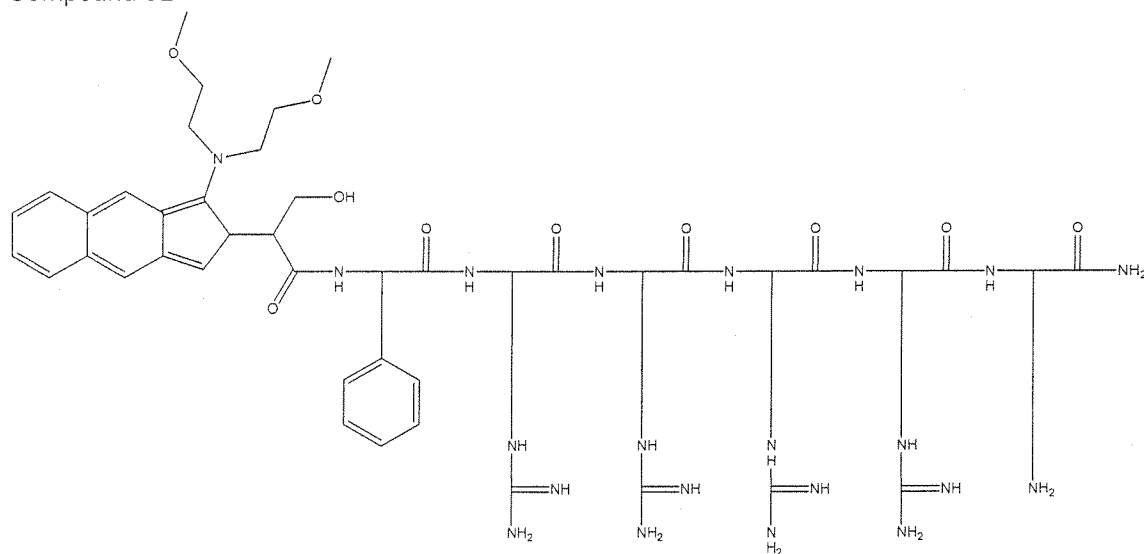


Compound 91

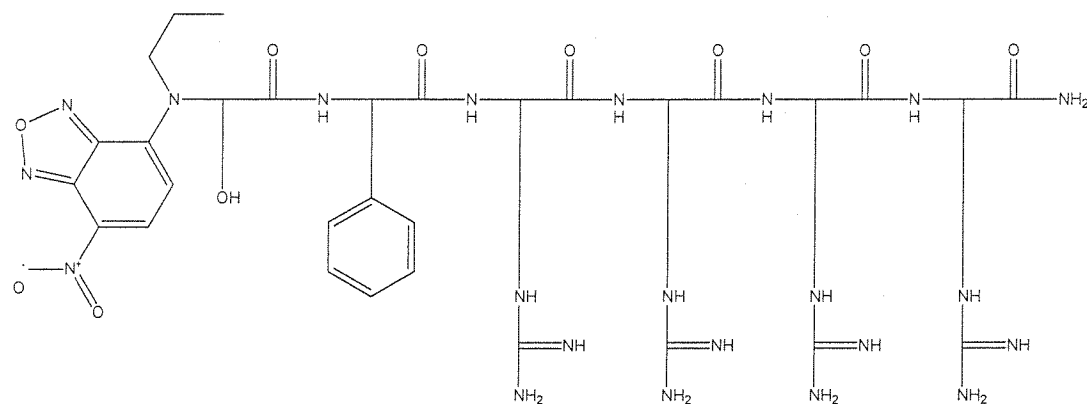
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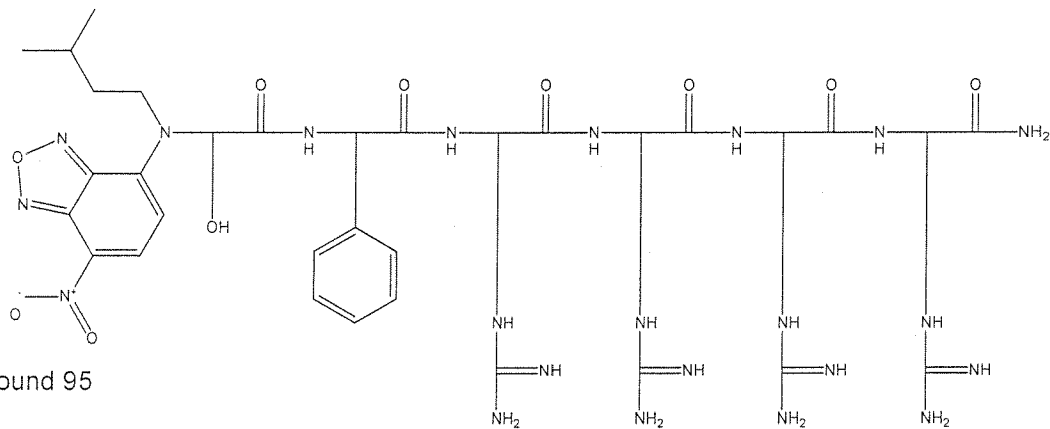
Compound 92



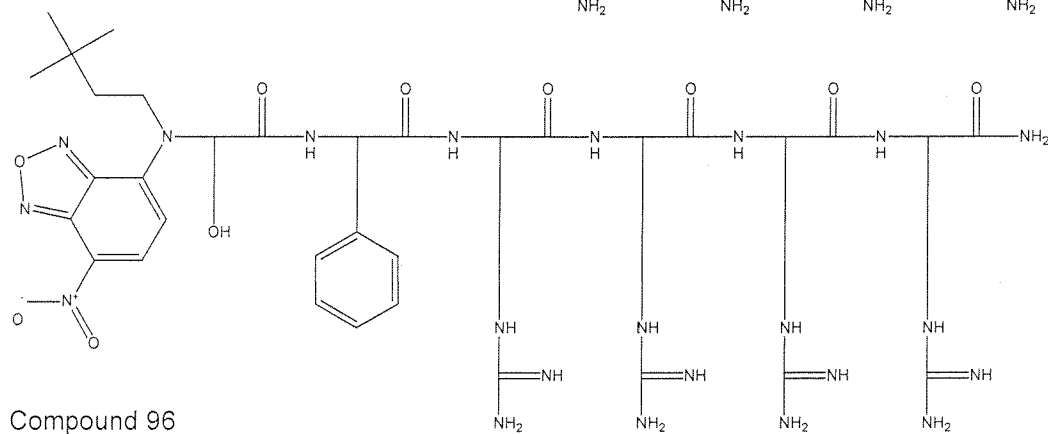
Compound 93



Compound 94



Compound 95



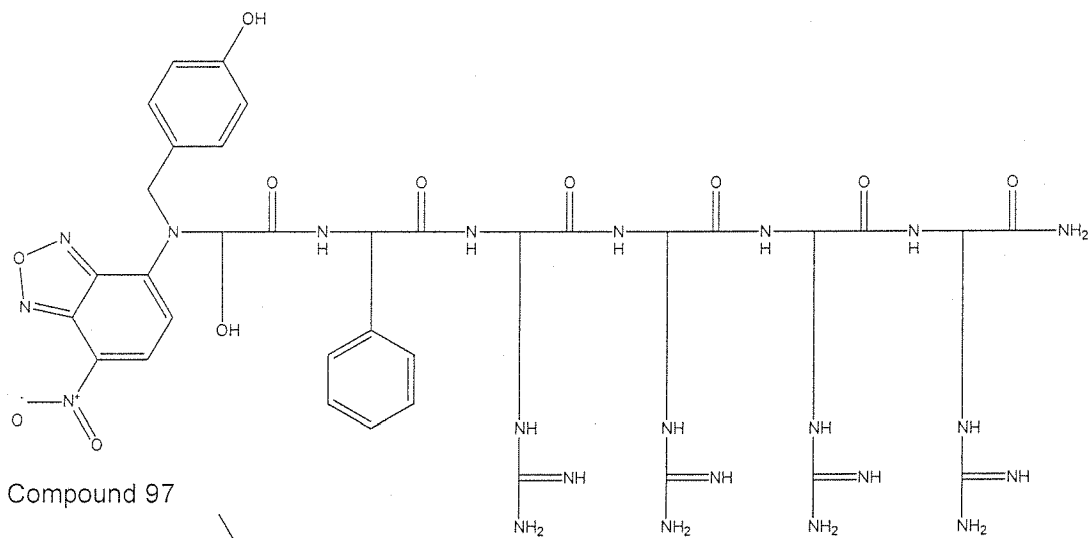
Compound 96

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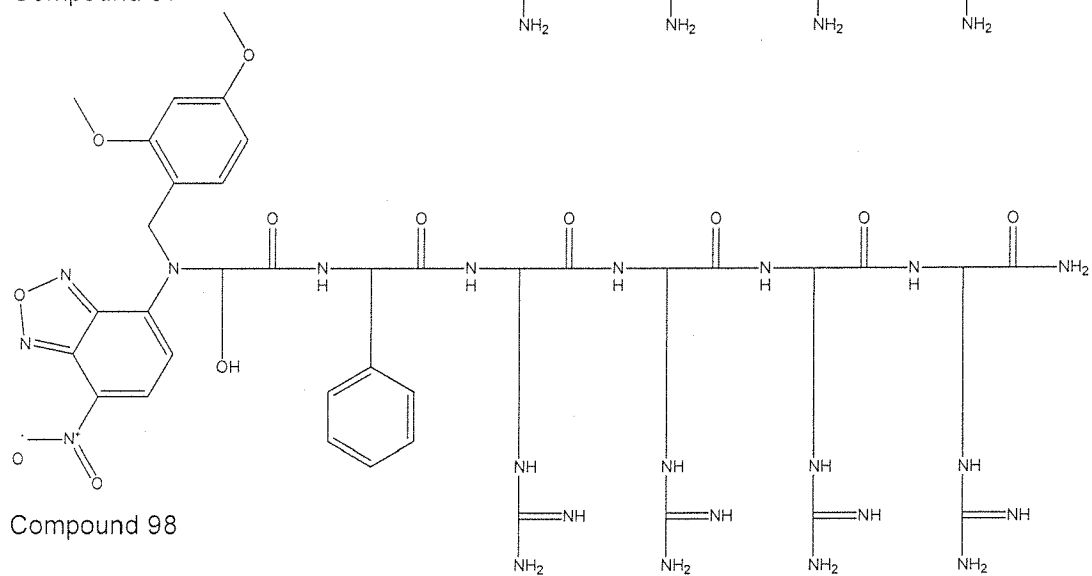
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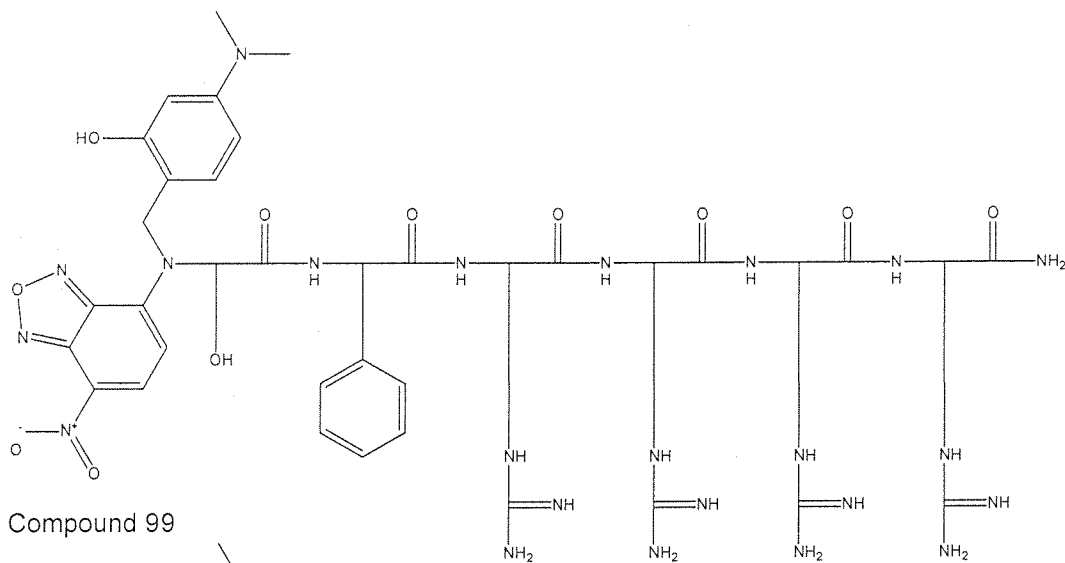


Compound 97

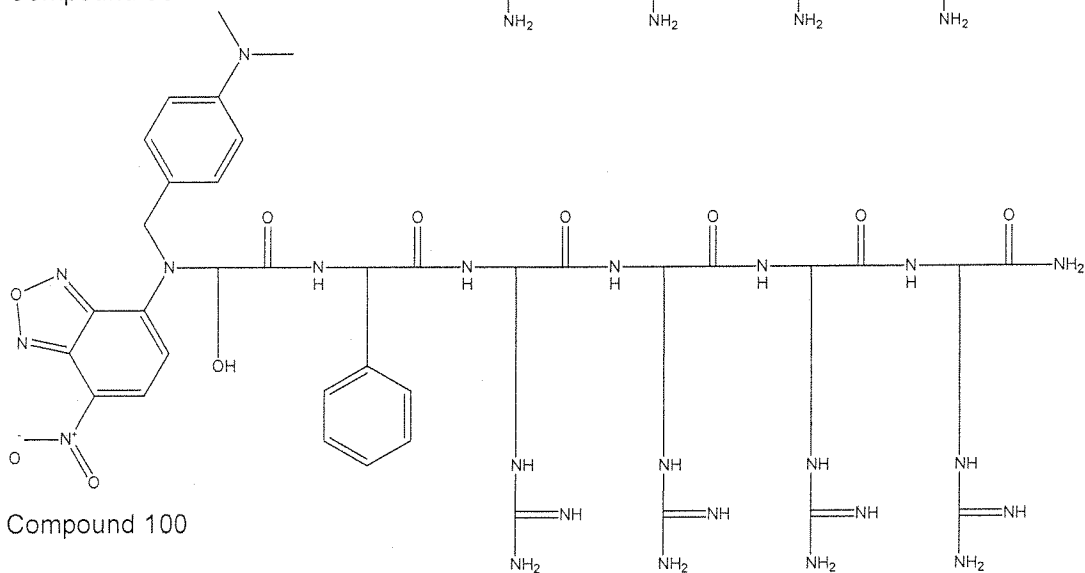


Compound 98

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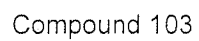
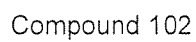
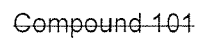


Compound 99

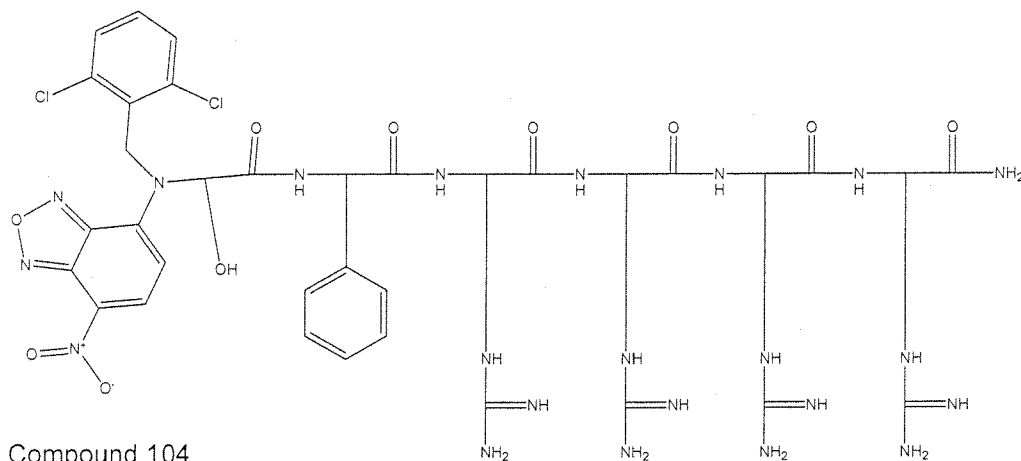


Compound 100

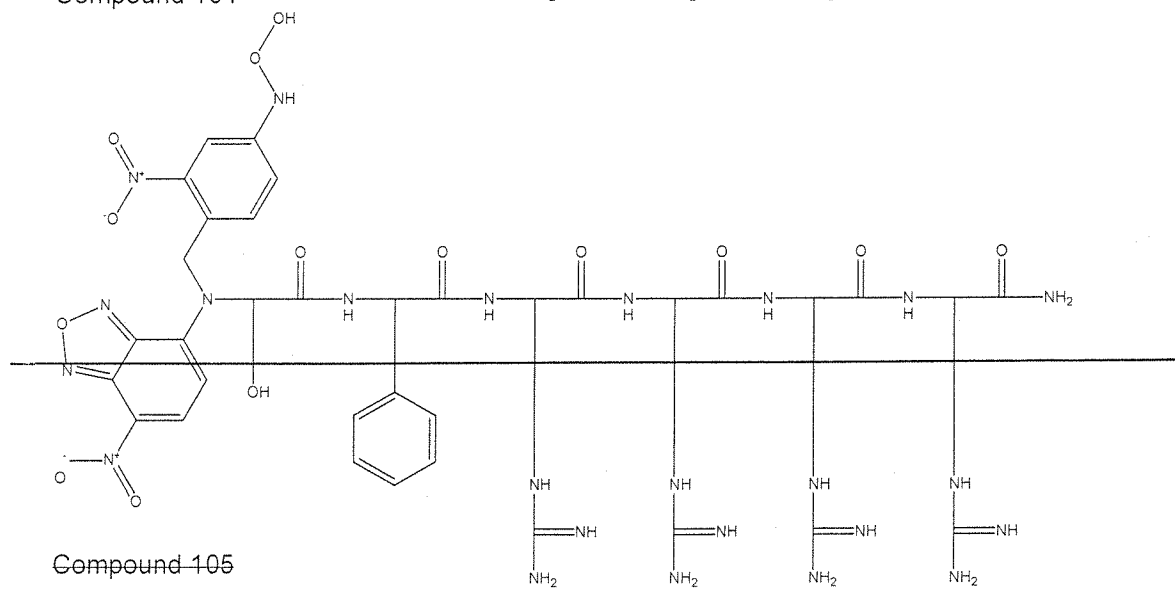
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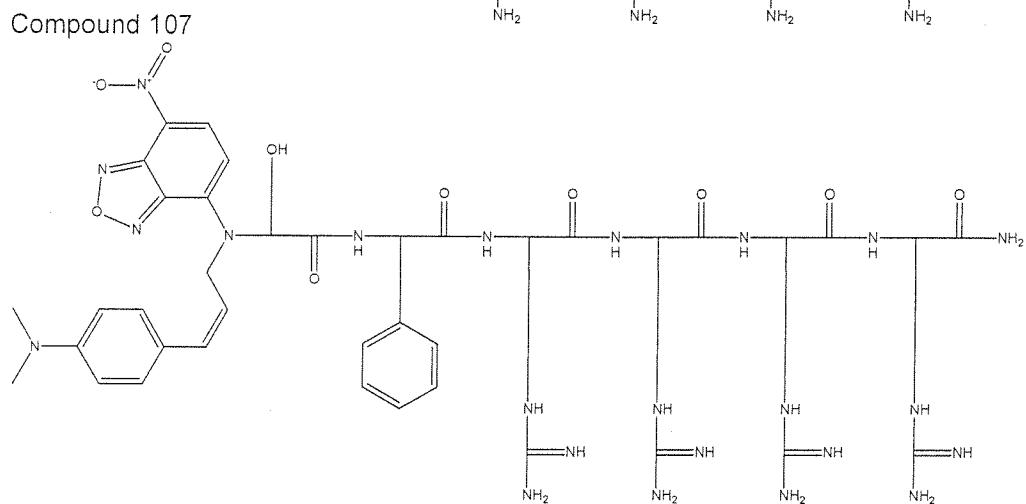
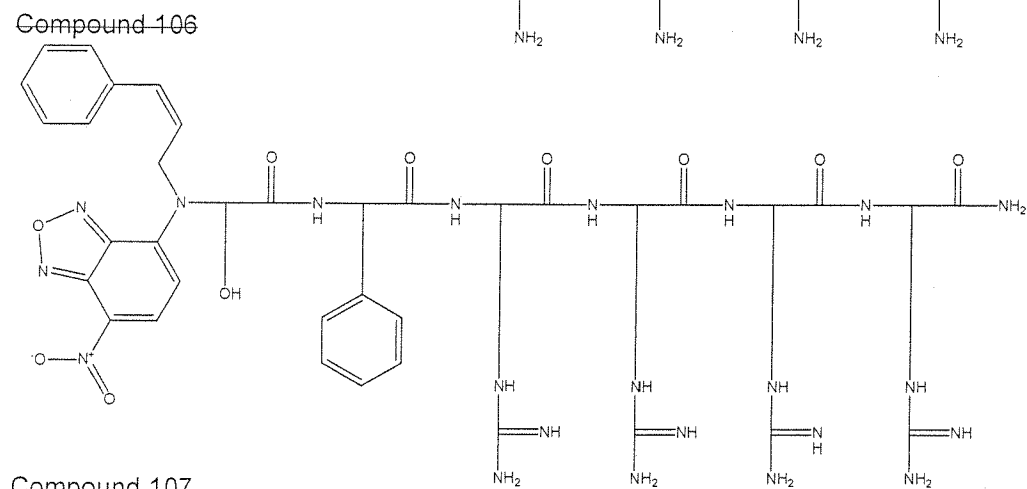
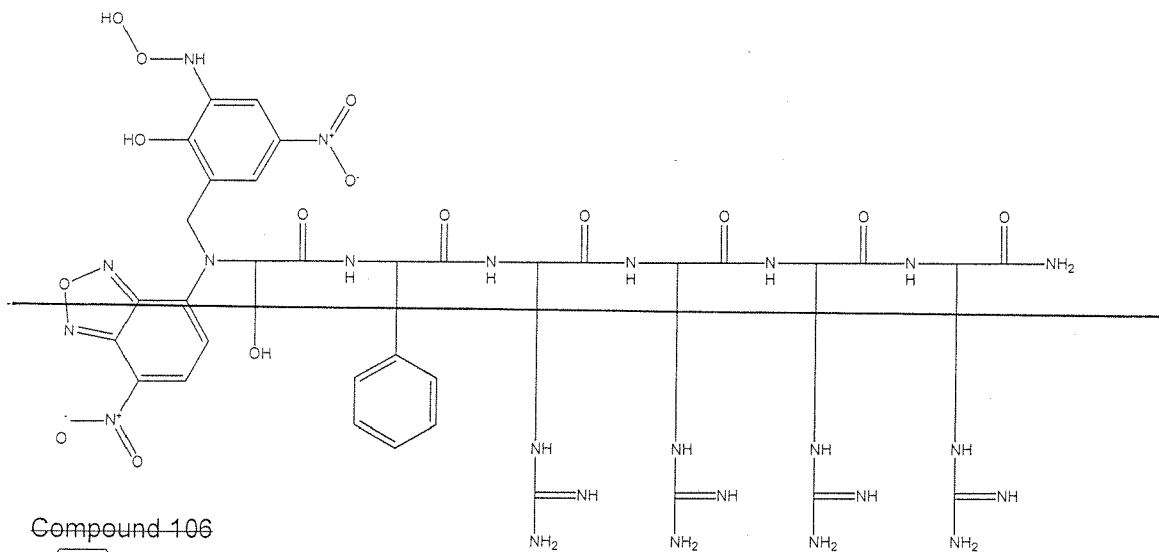


Compound 104

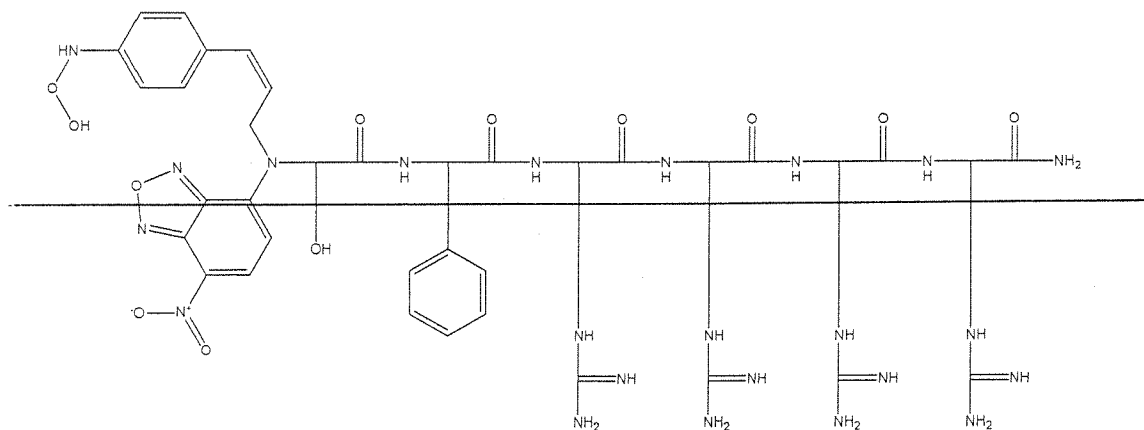
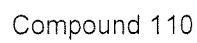


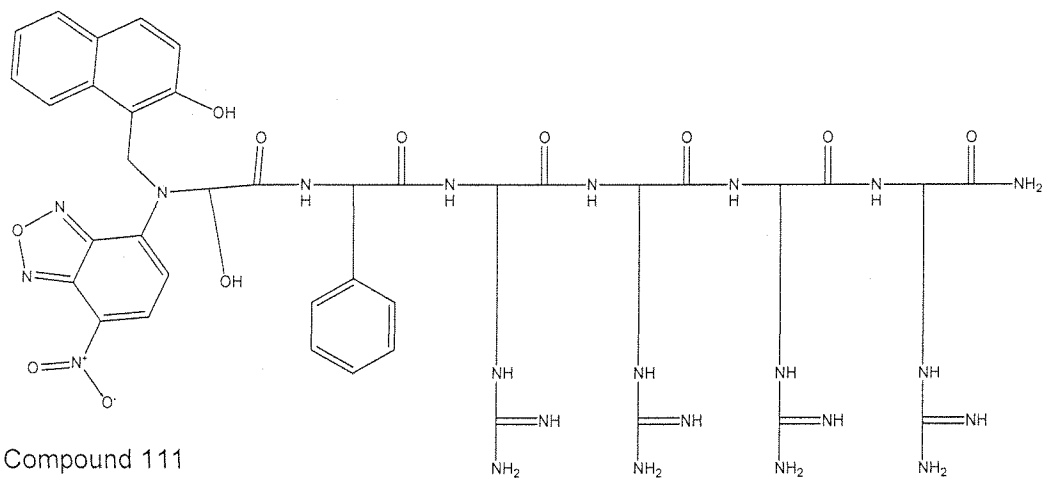
Compound 105

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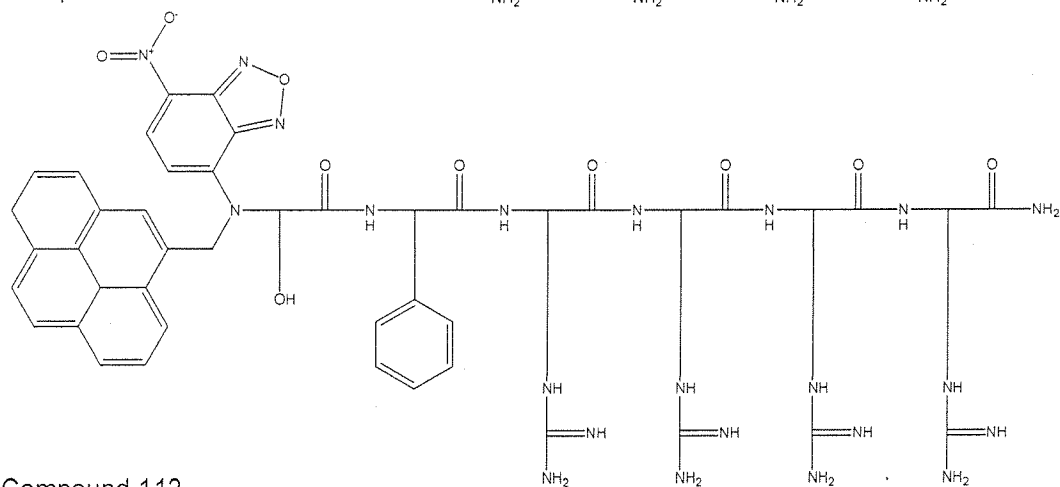


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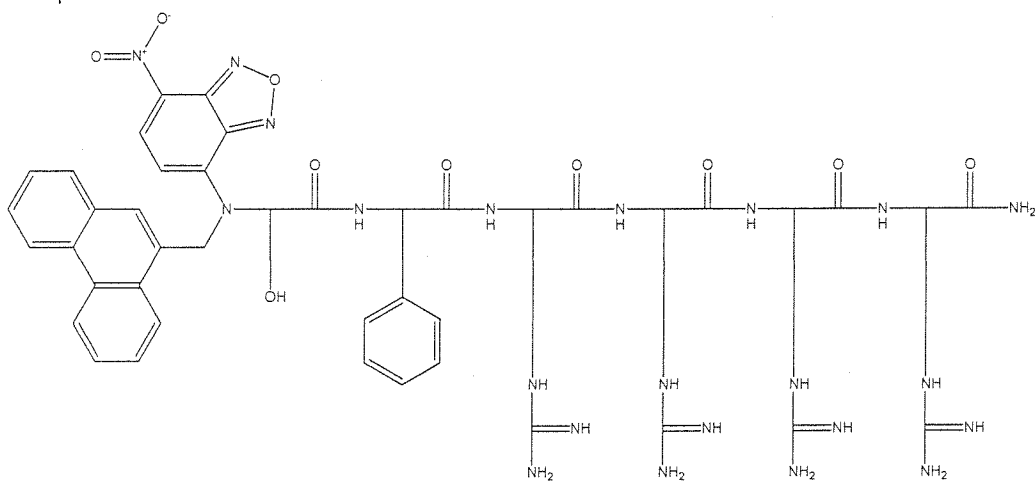
O=C(N)C(O)CN(c1ccc(cc1)/C=C/c2ccccc2)c3cc4c(cc3[N+]([O-])=O)c5nnoc54



Compound 111

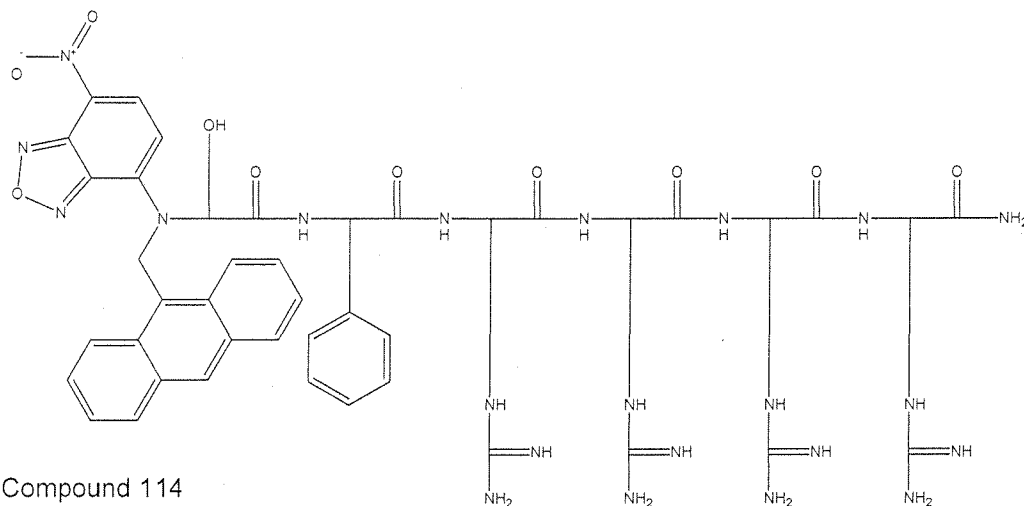


Compound 112

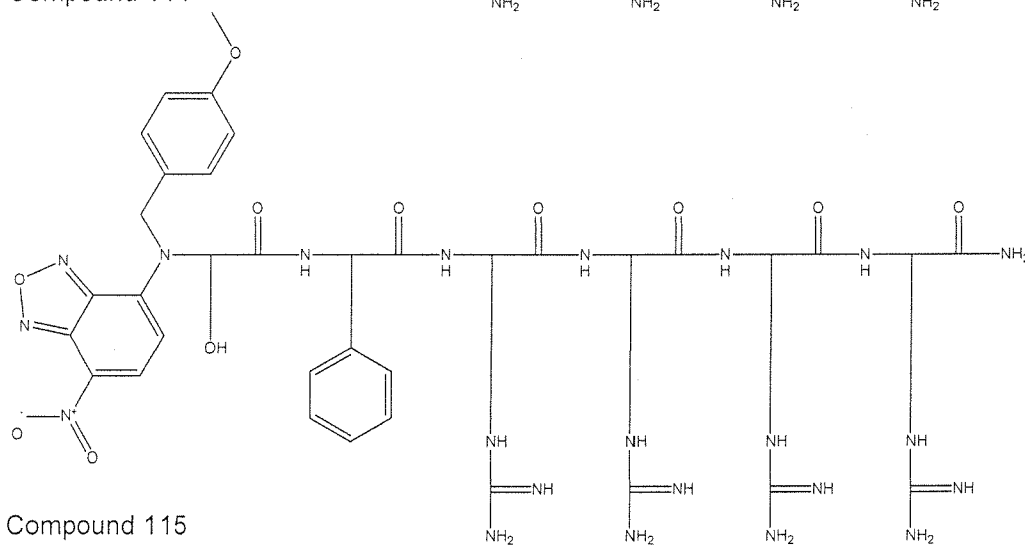


Compound 113

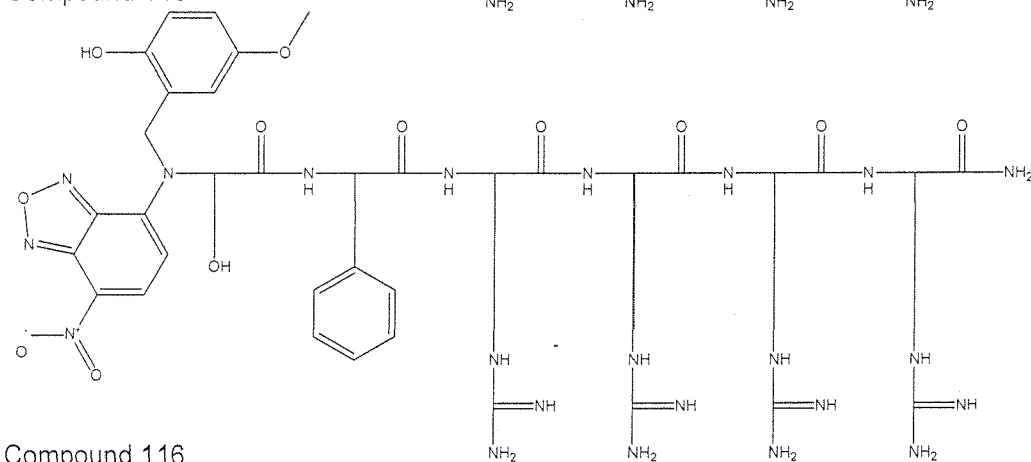
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Compound 114

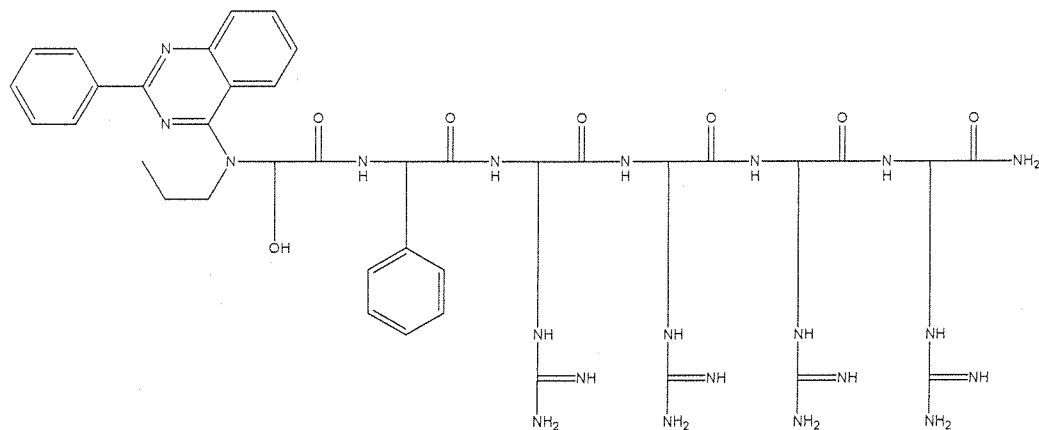


Compound 115

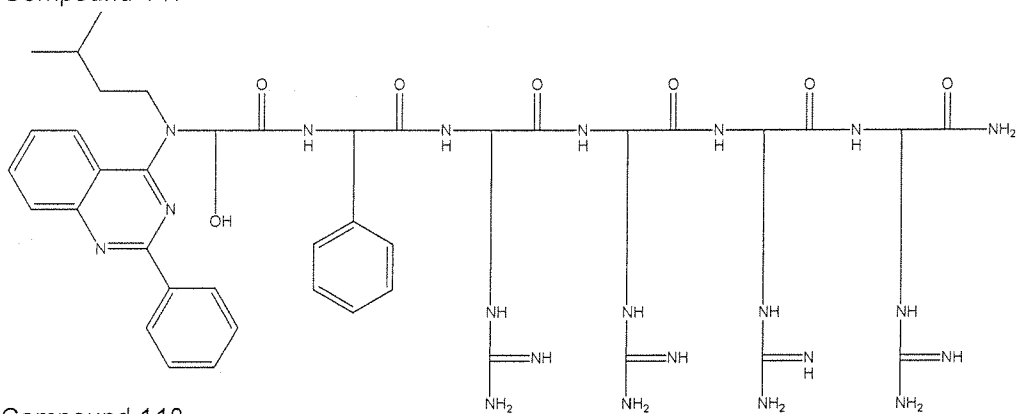


Compound 116

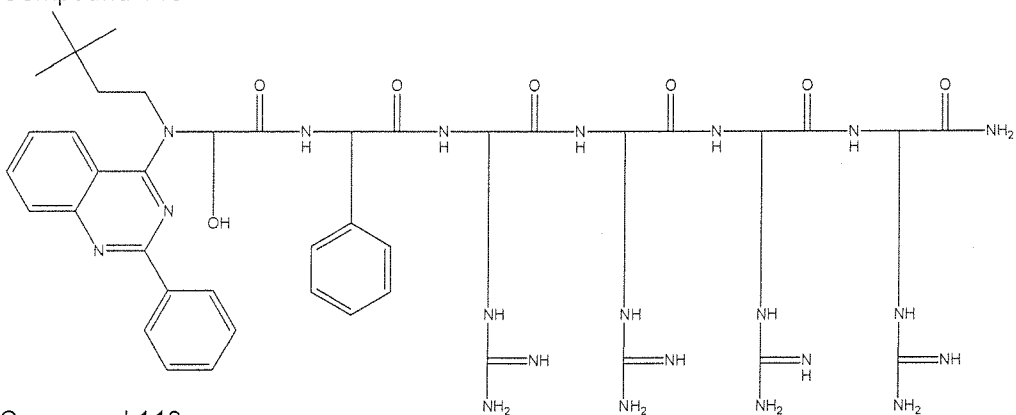
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Compound 117



Compound 118



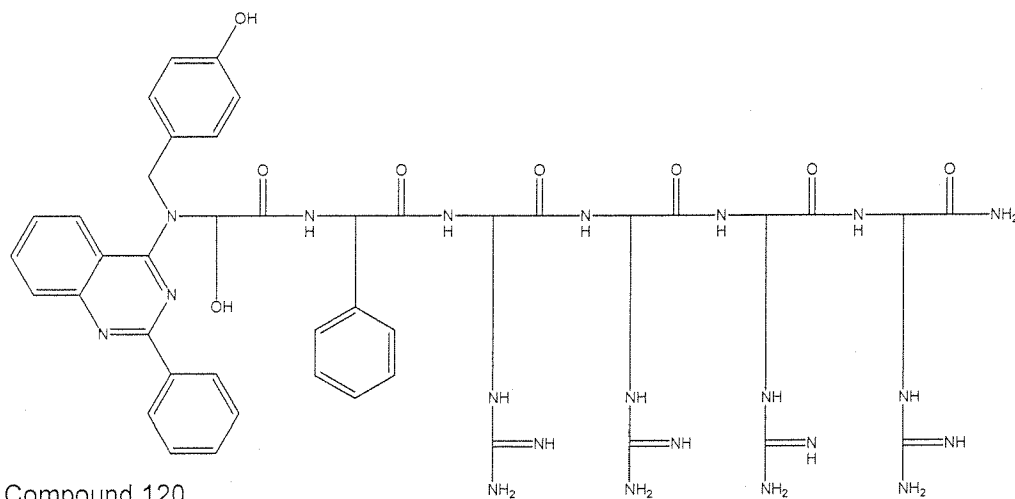
Compound 119

Applicant: David S. Lawrence

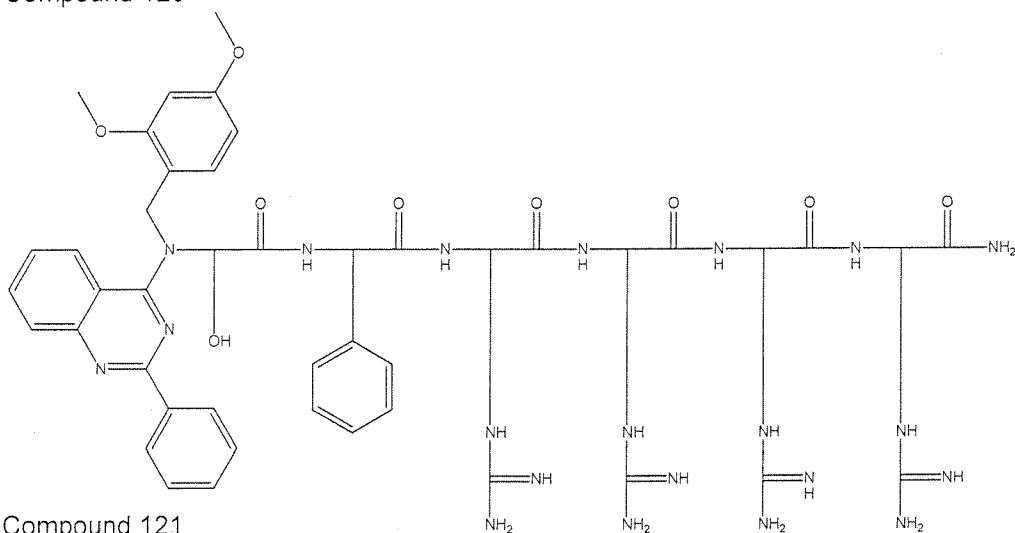
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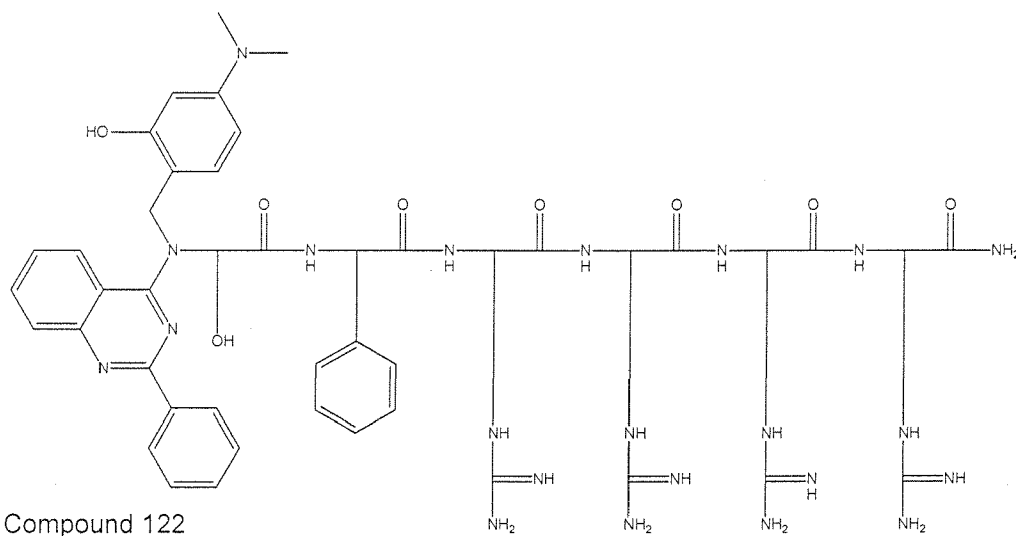


Compound 120

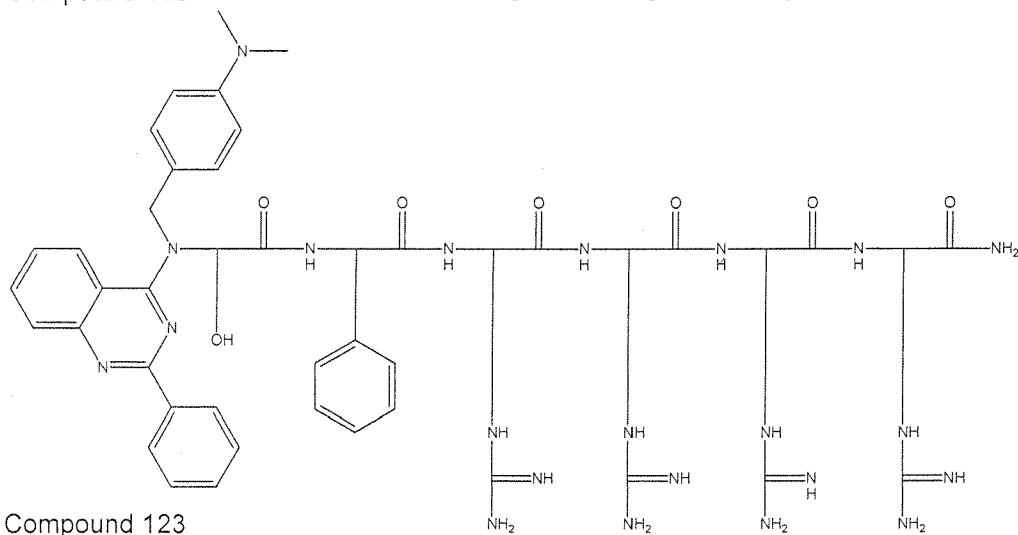


Compound 121

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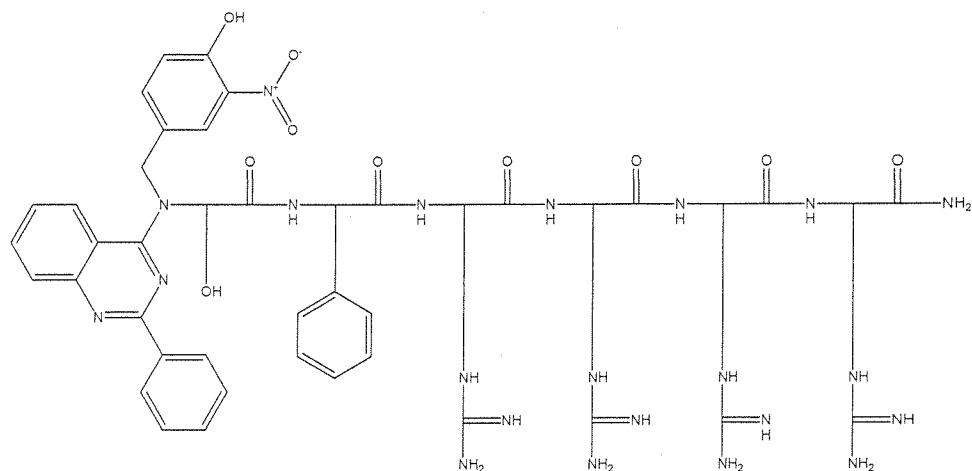
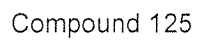
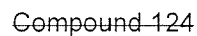


Compound 122

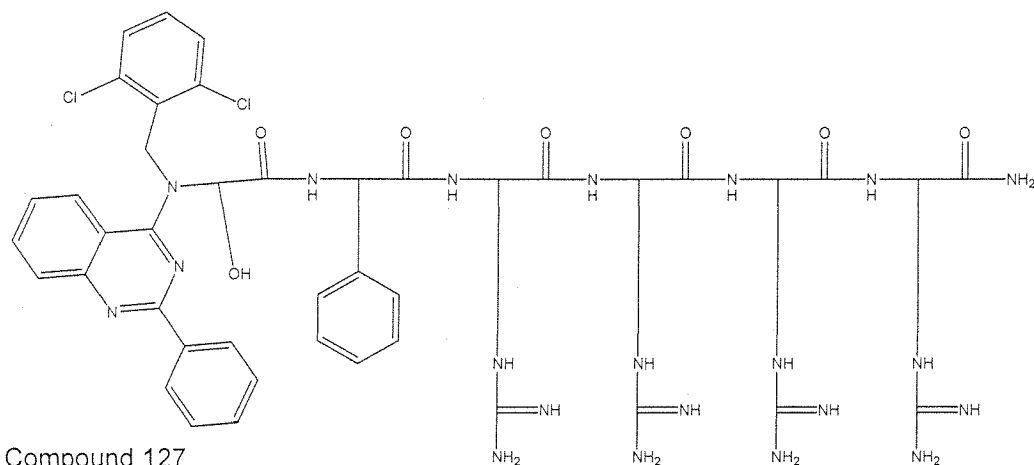


Compound 123

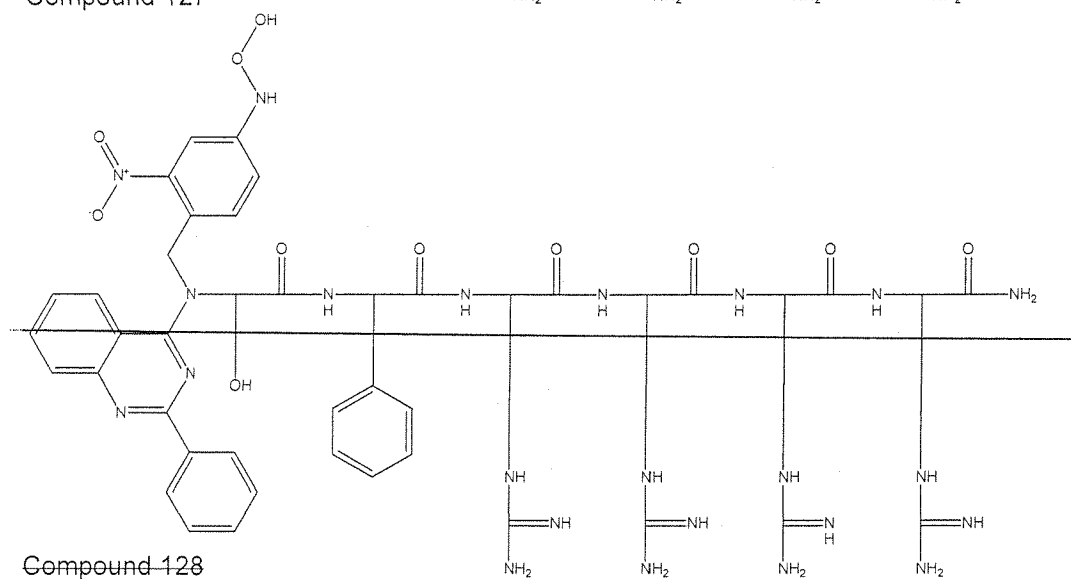
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Compound 127



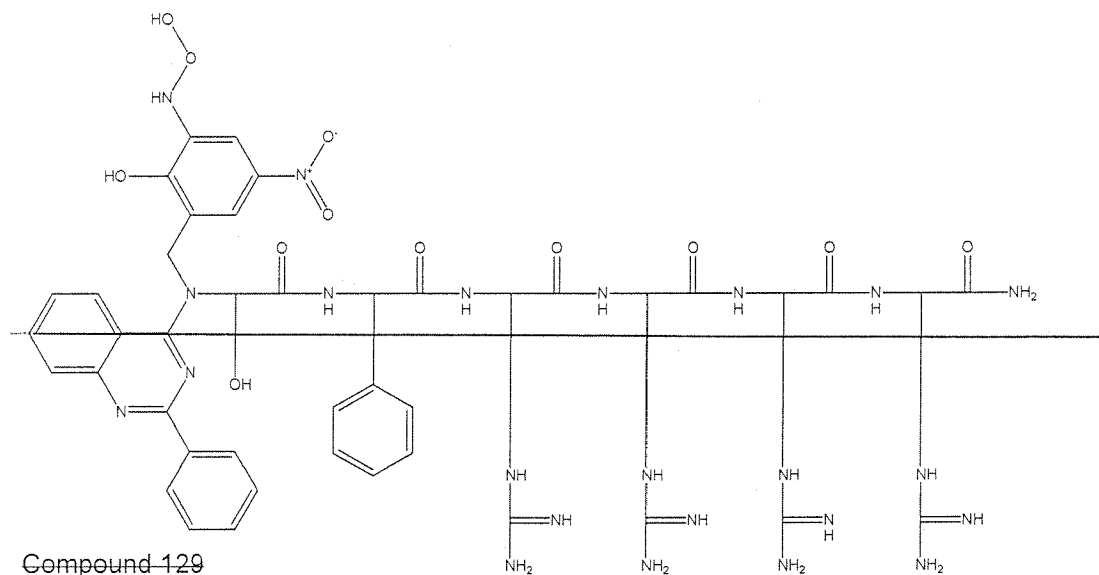
Compound 128

Applicant: David S. Lawrence

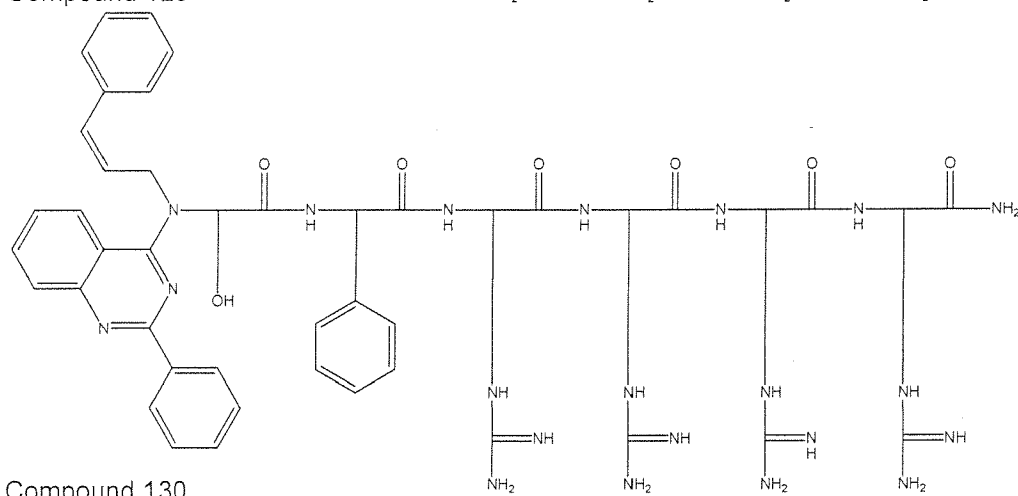
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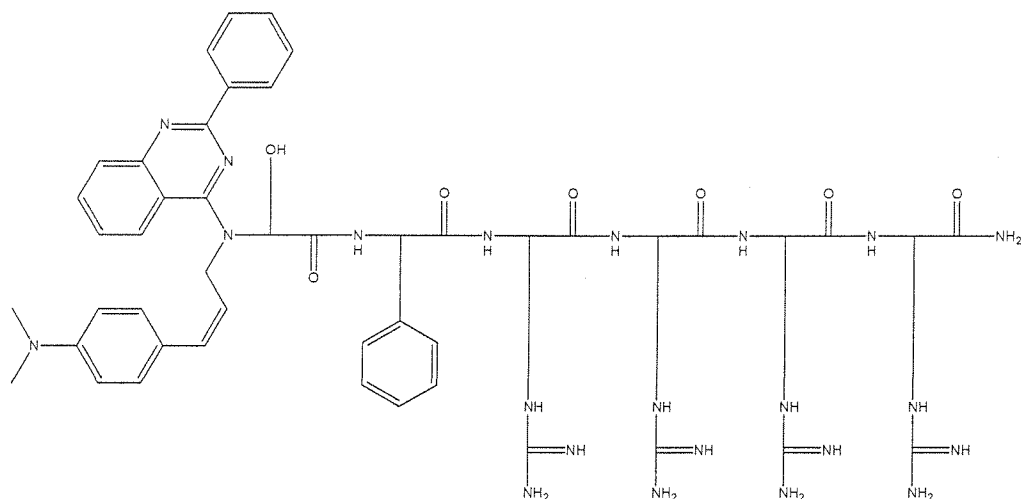


Compound 129

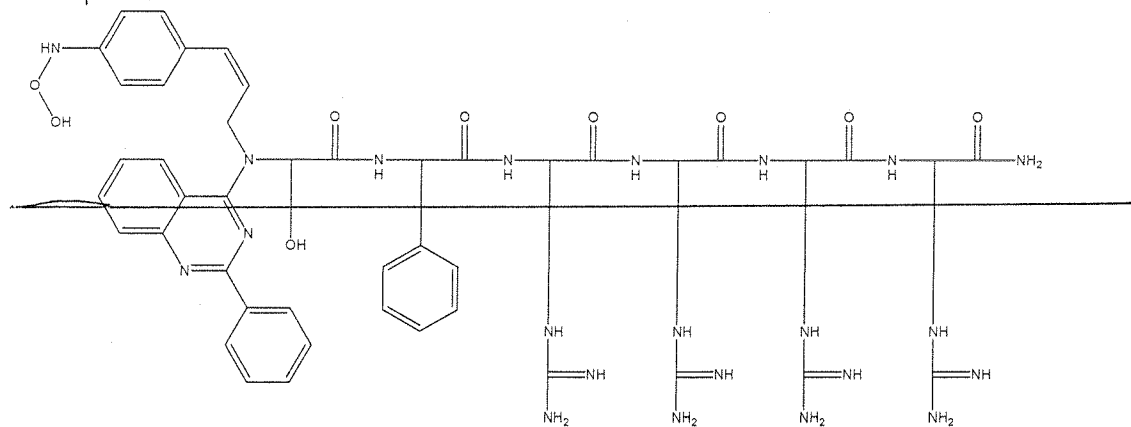


Compound 130

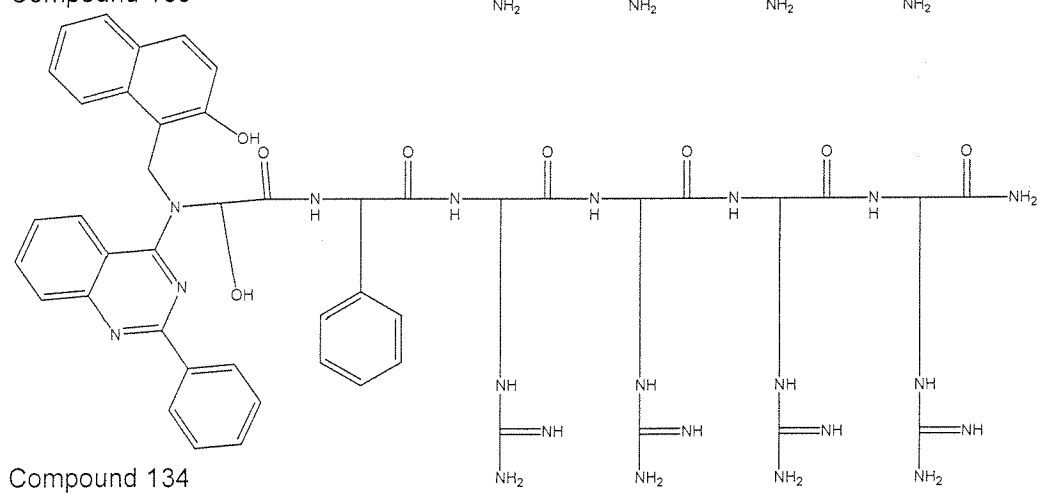
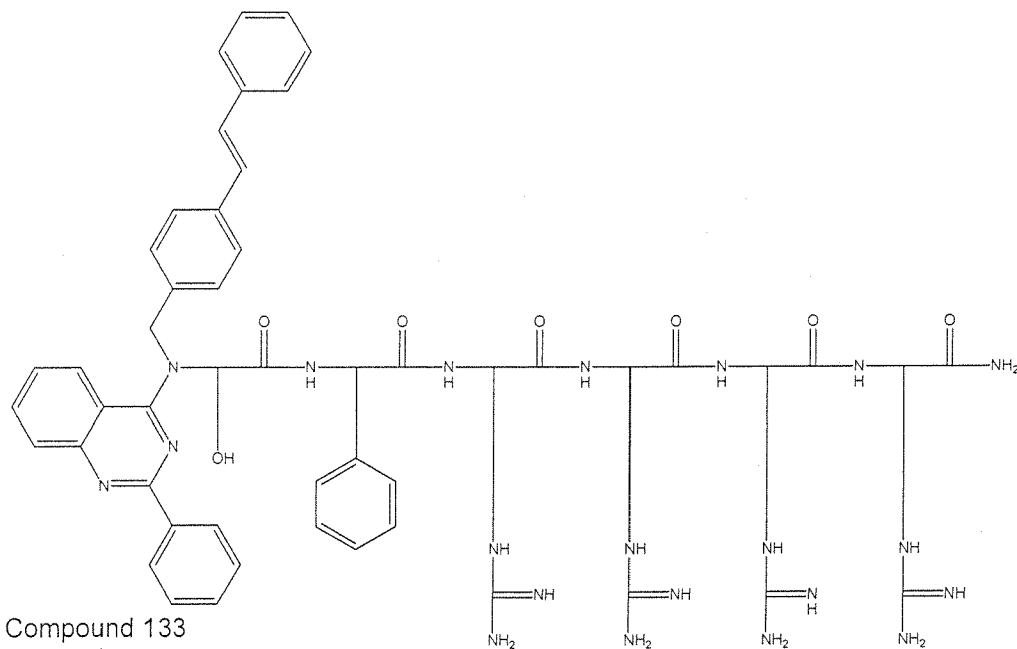
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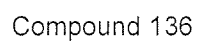
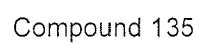
Compound 131



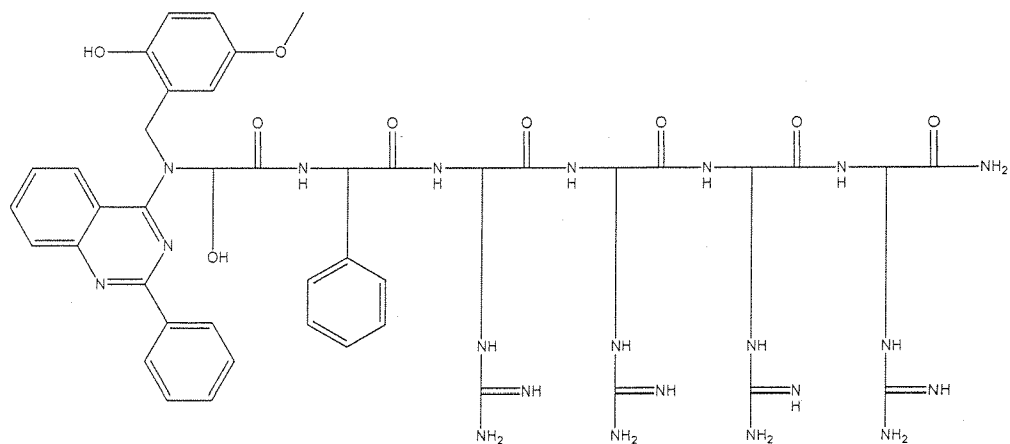
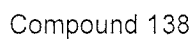
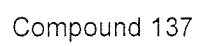
Compound 132

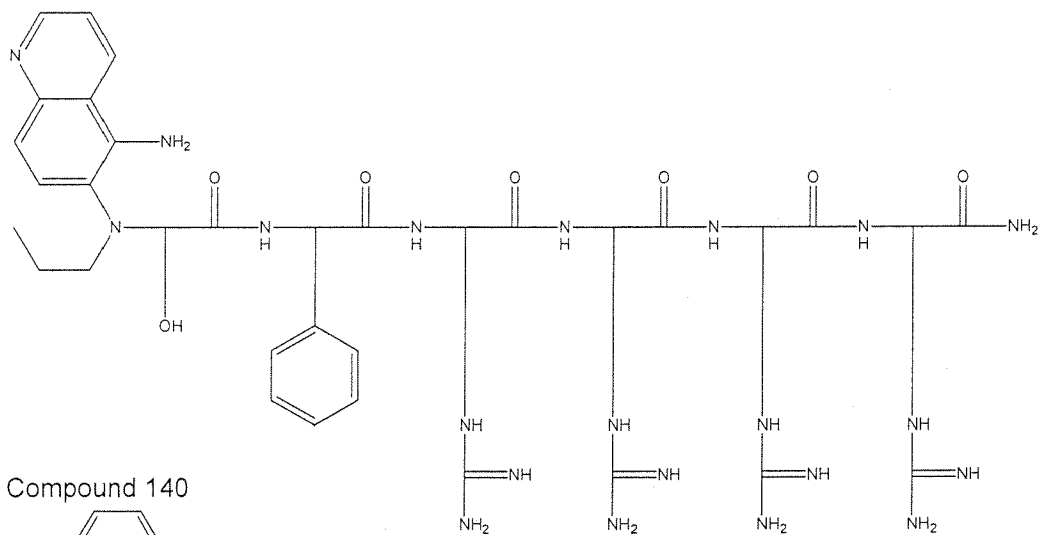


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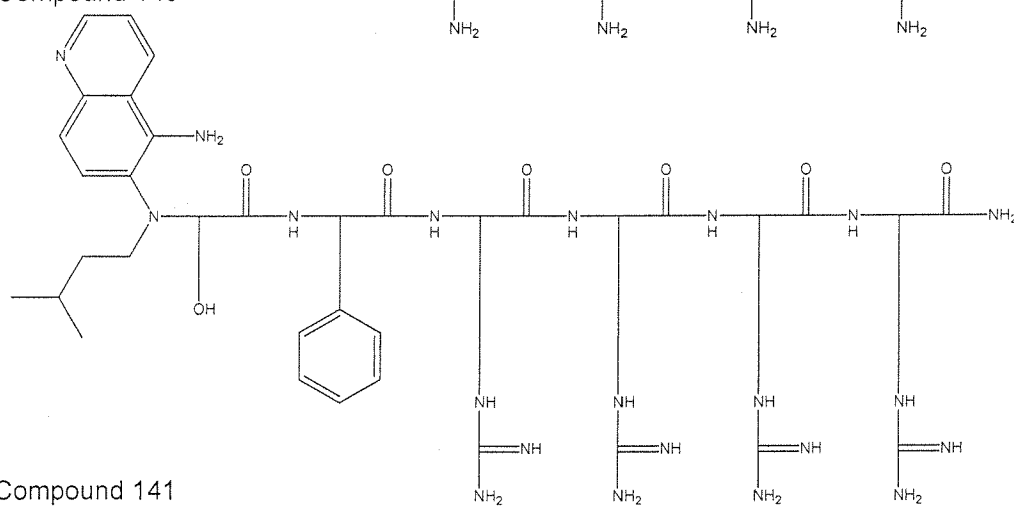


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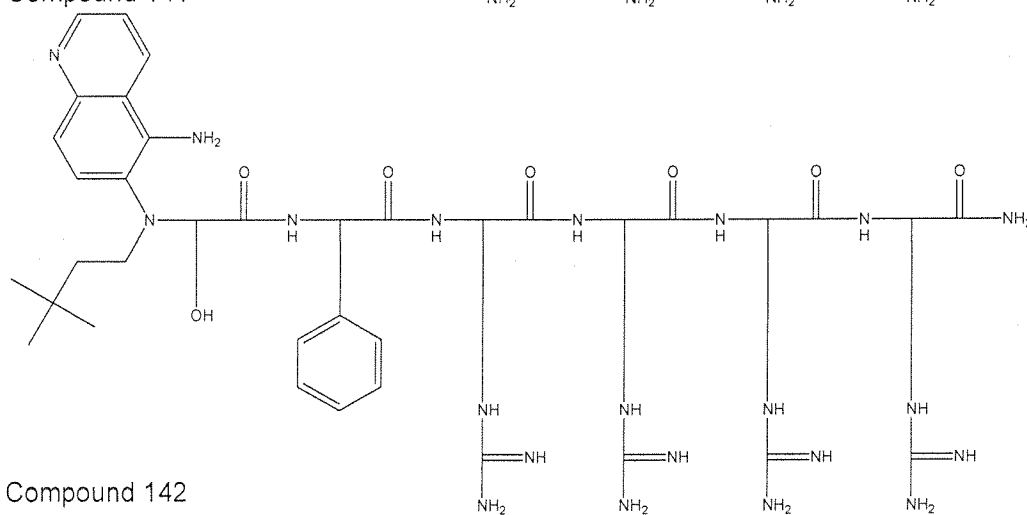




Compound 140



Compound 141



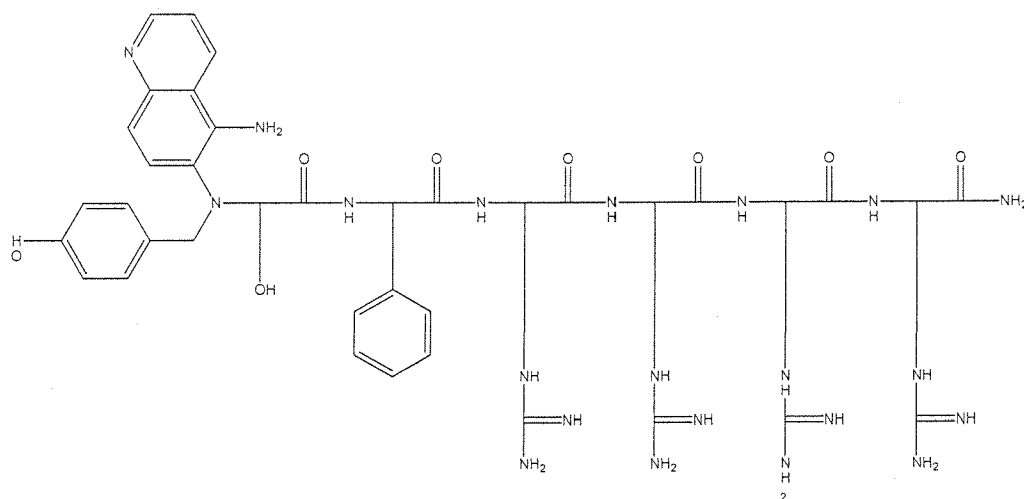
Compound 142

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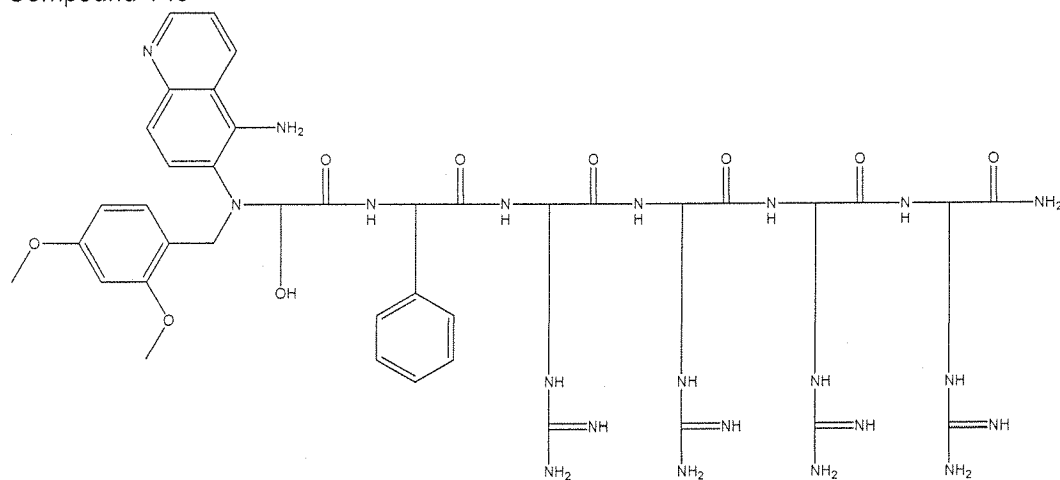
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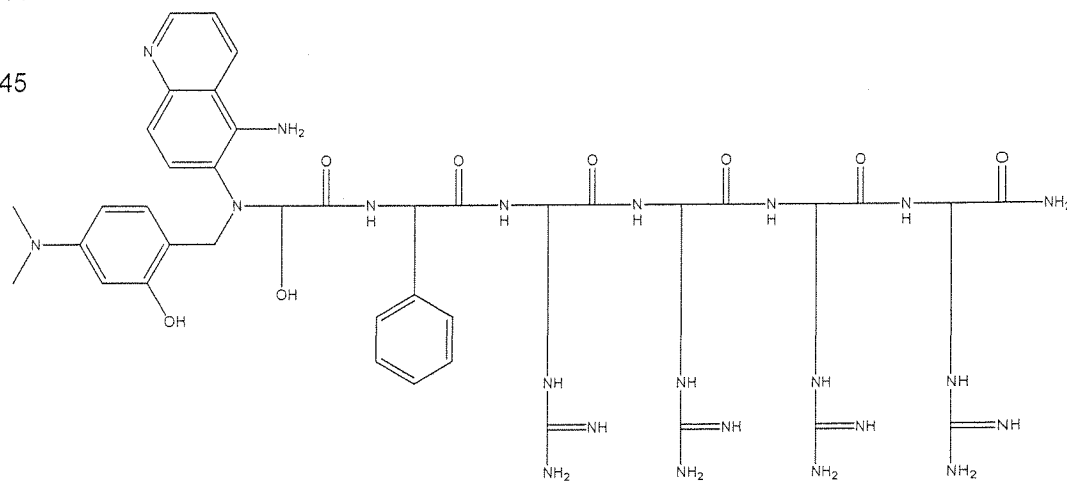


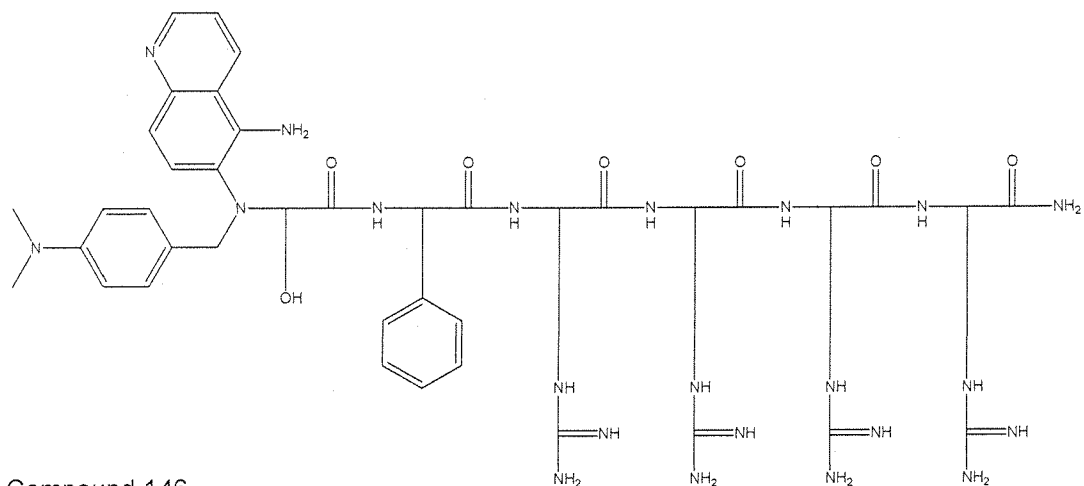
Compound 143



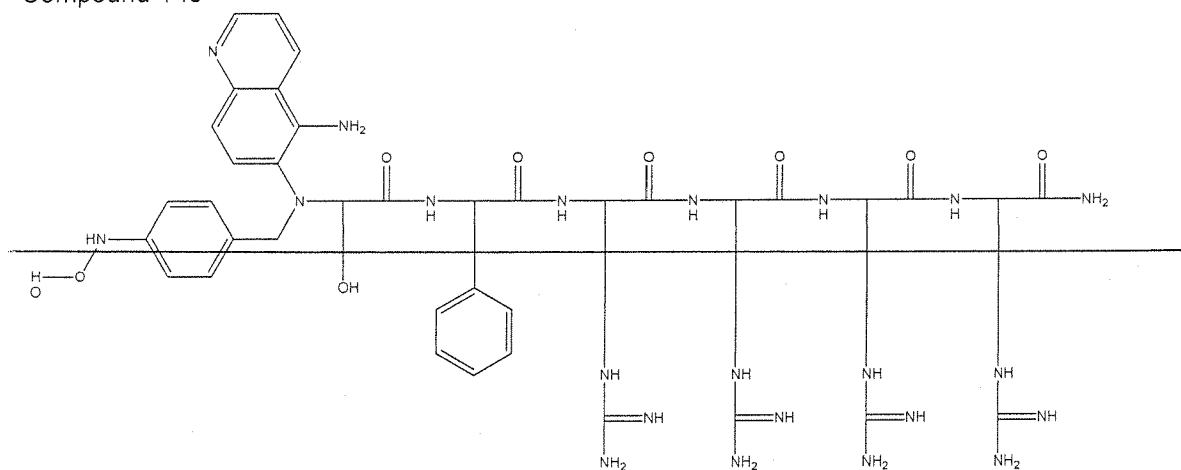
Compound 144

Compound 145

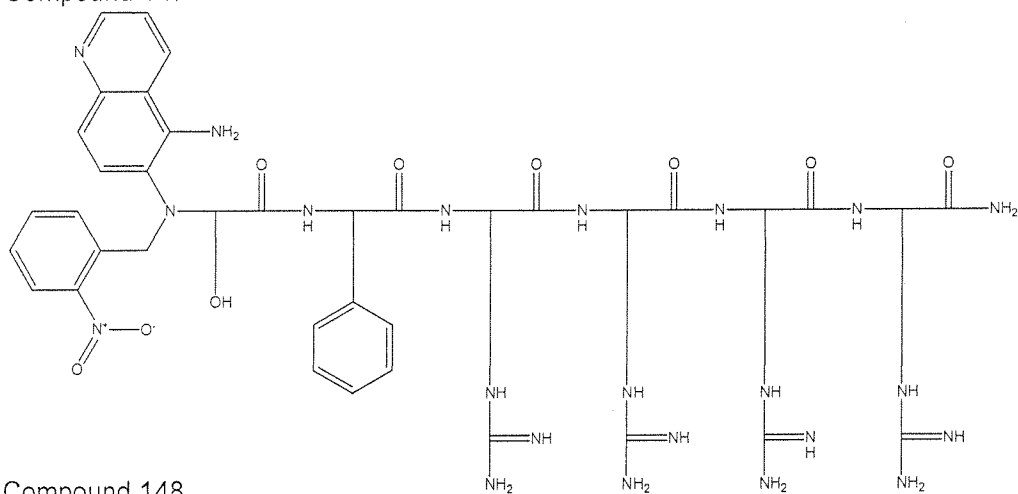




Compound 146

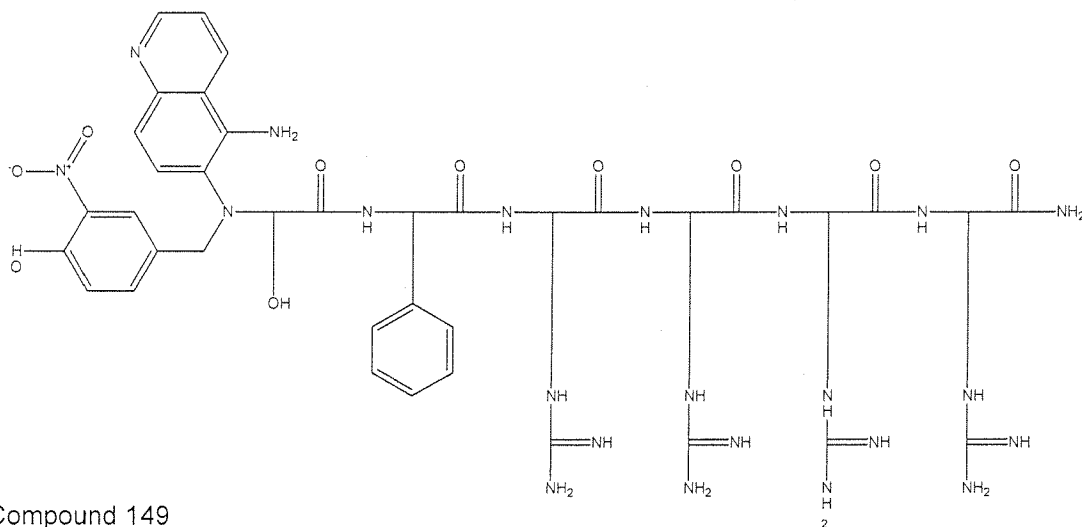


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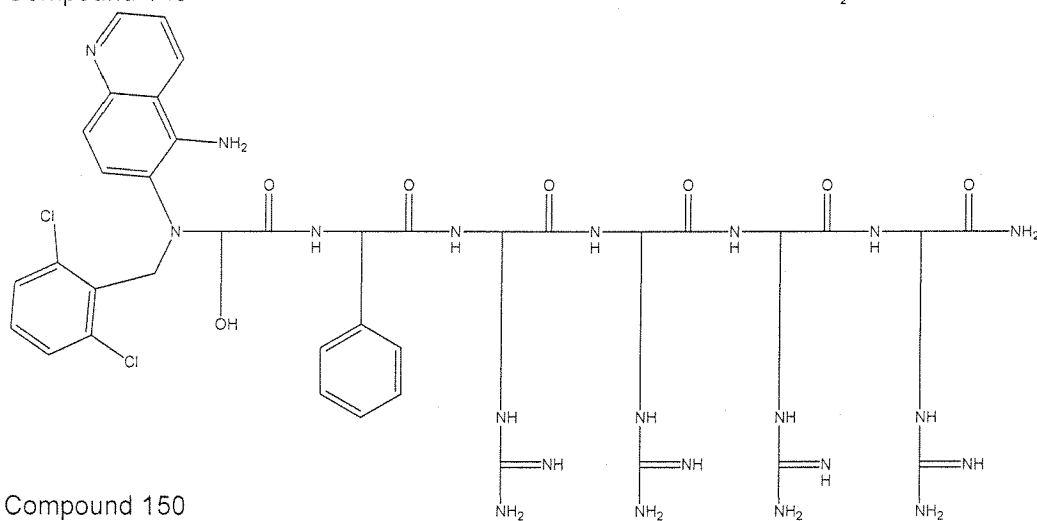


Compound 148

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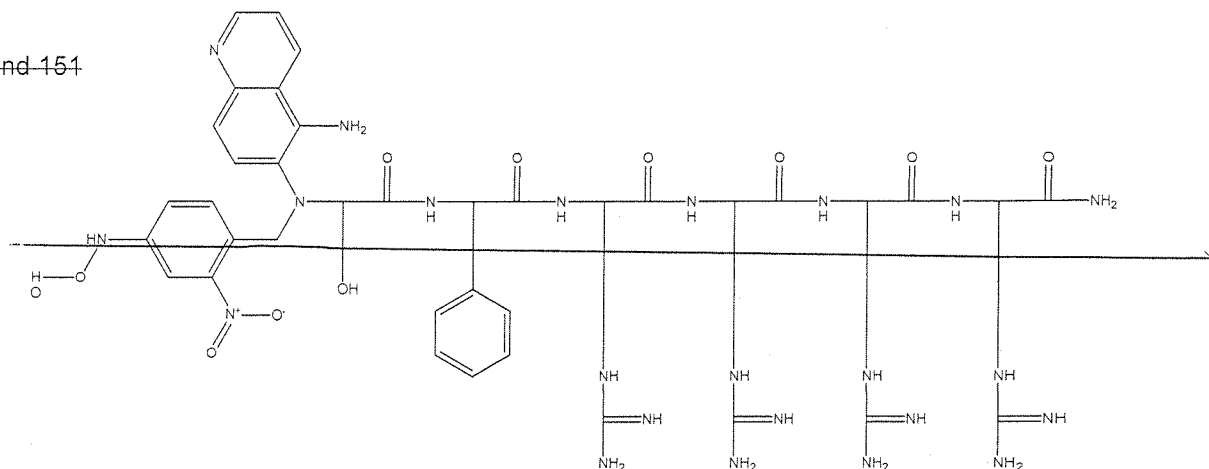


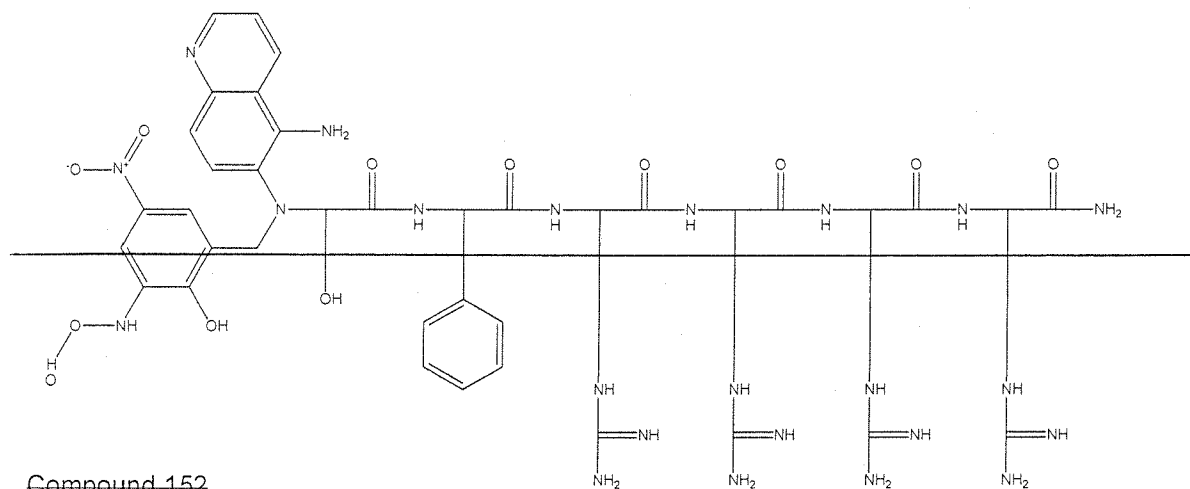
Compound 149



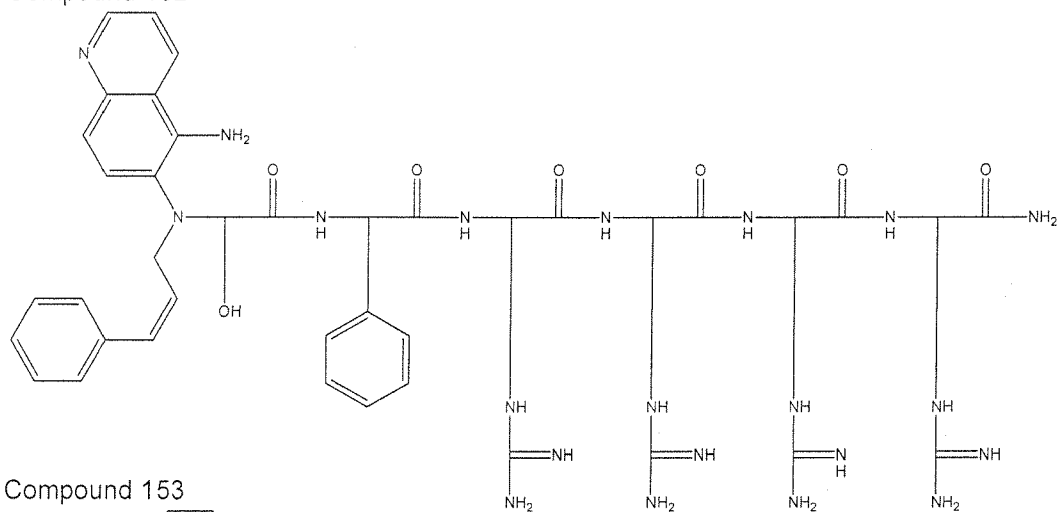
Compound 150

Compound 151

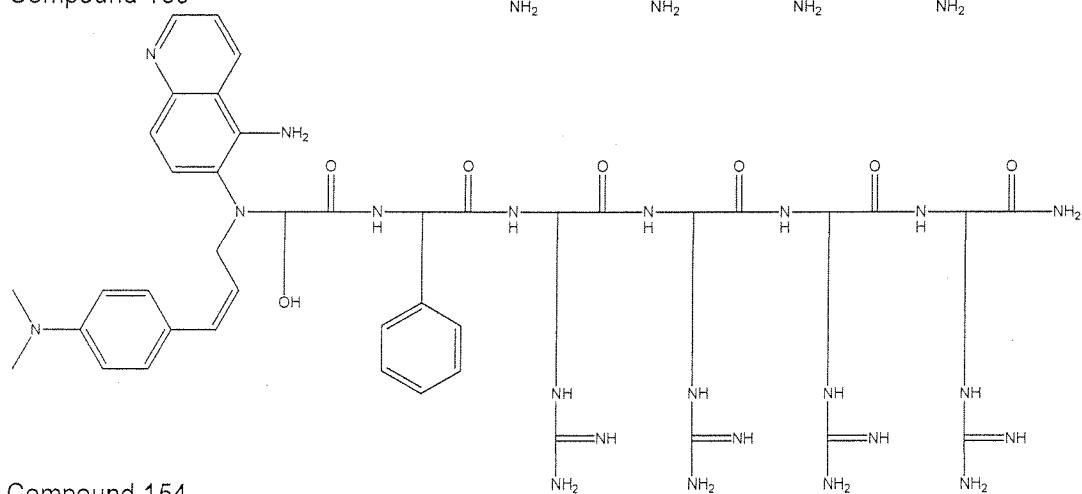




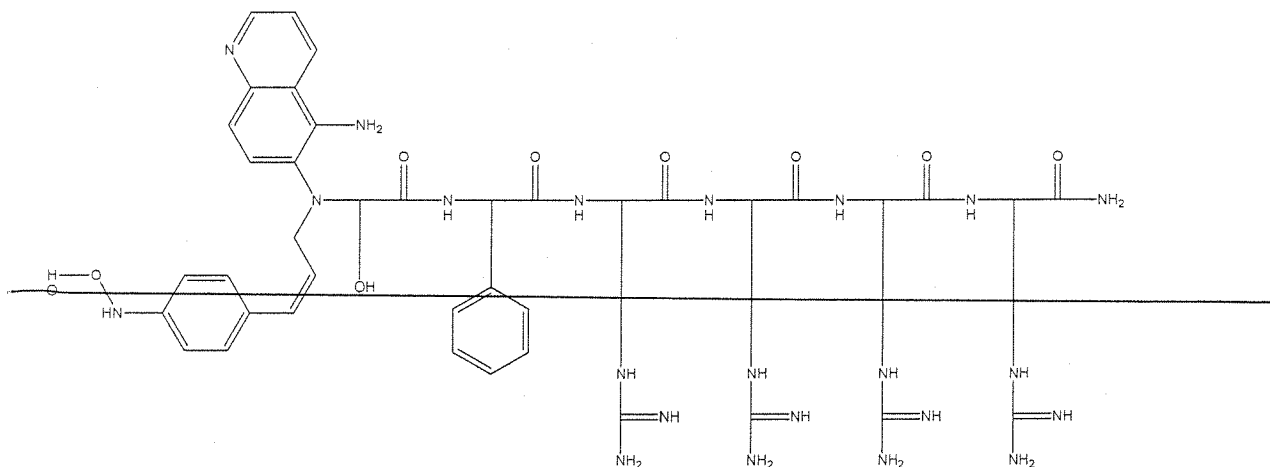
Compound 152



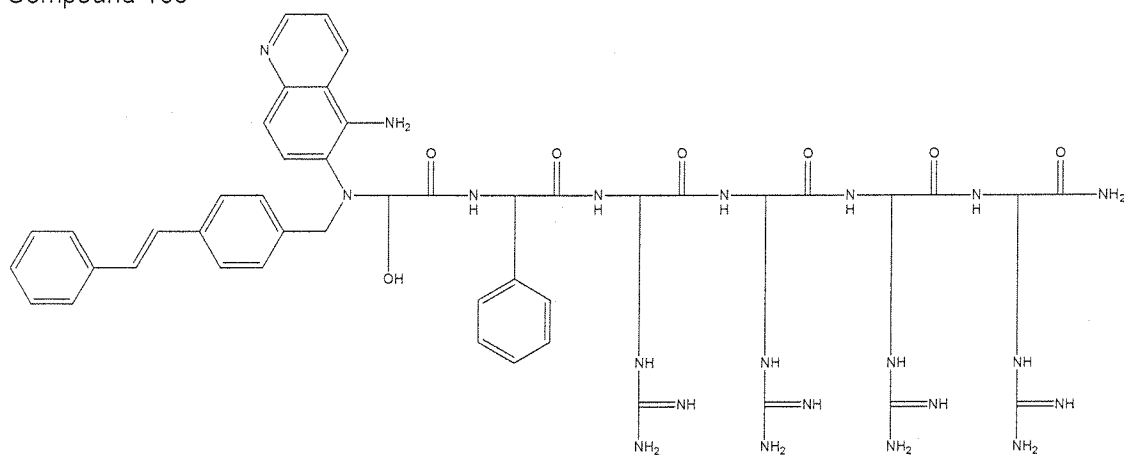
Compound 153



Compound 154

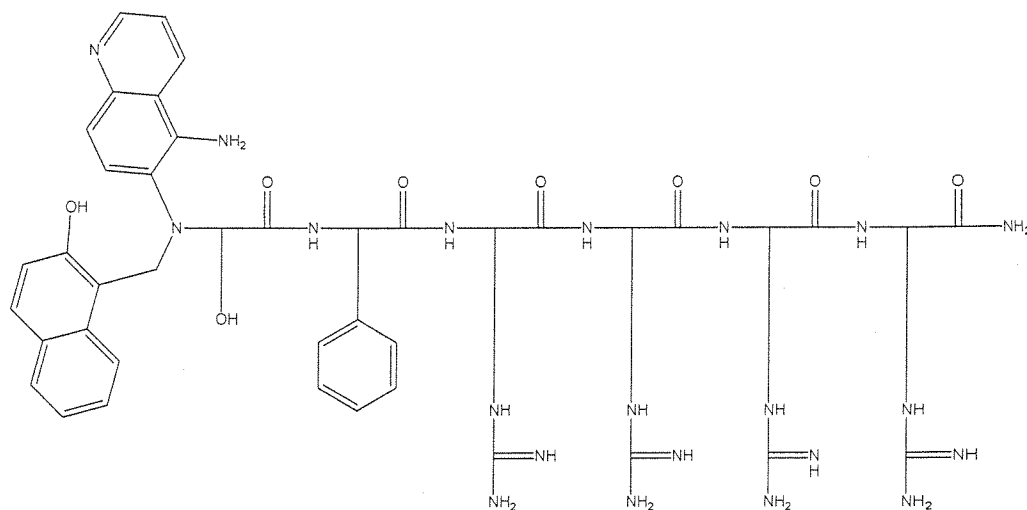


Compound 155

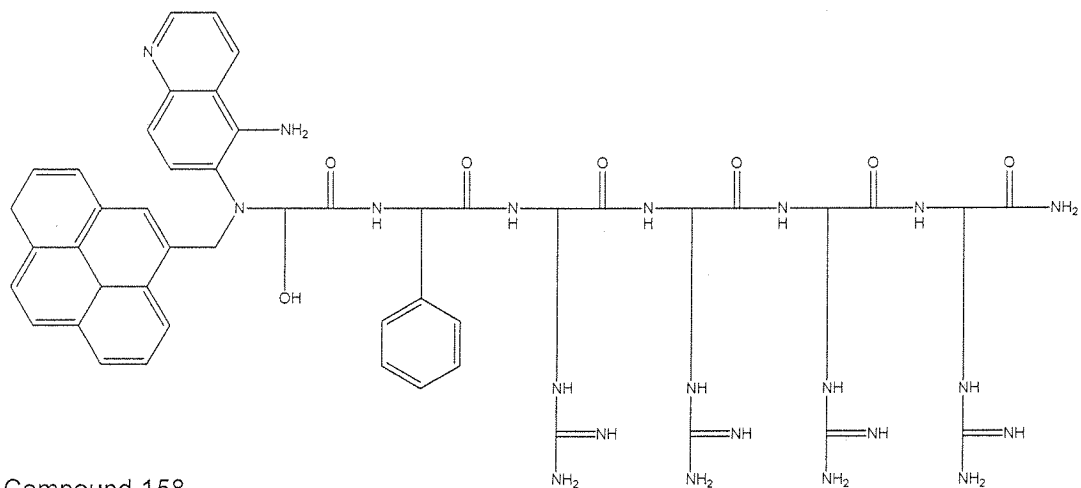


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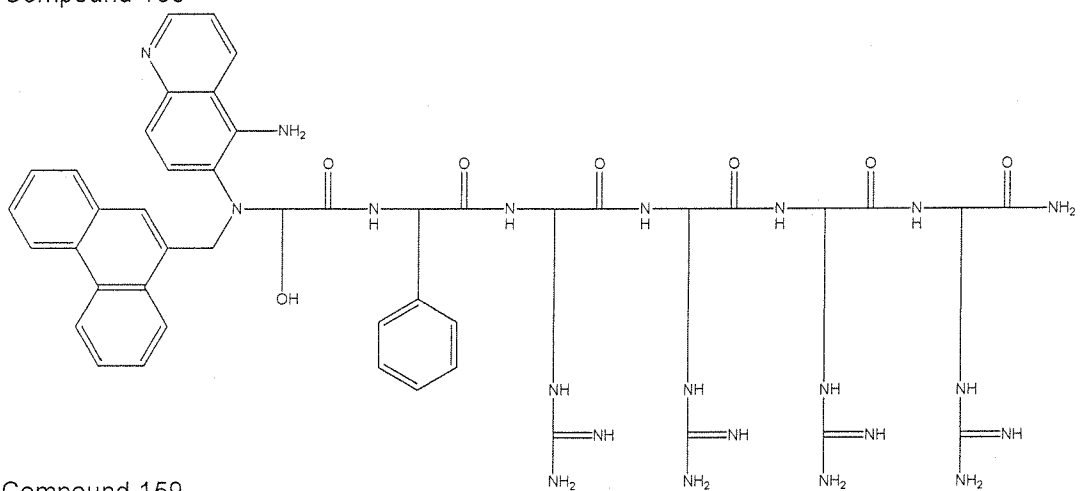
Compound 157



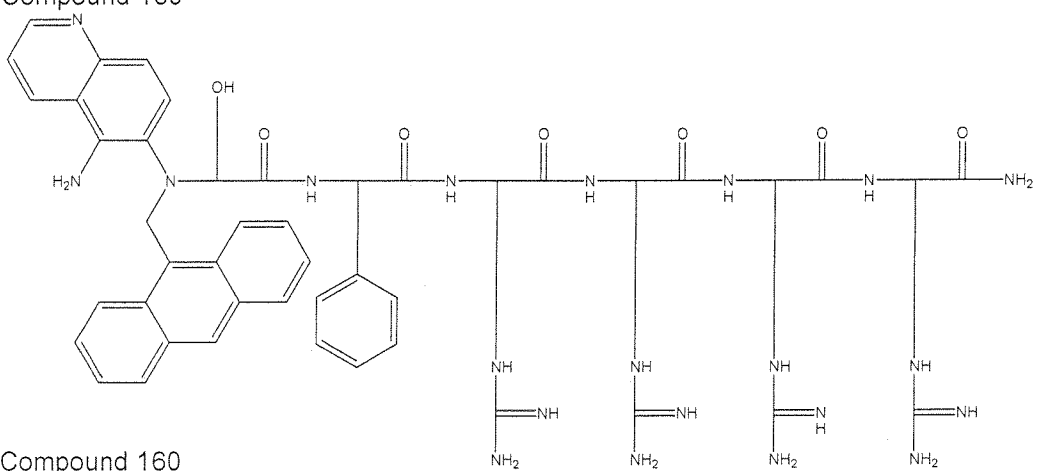
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Compound 158

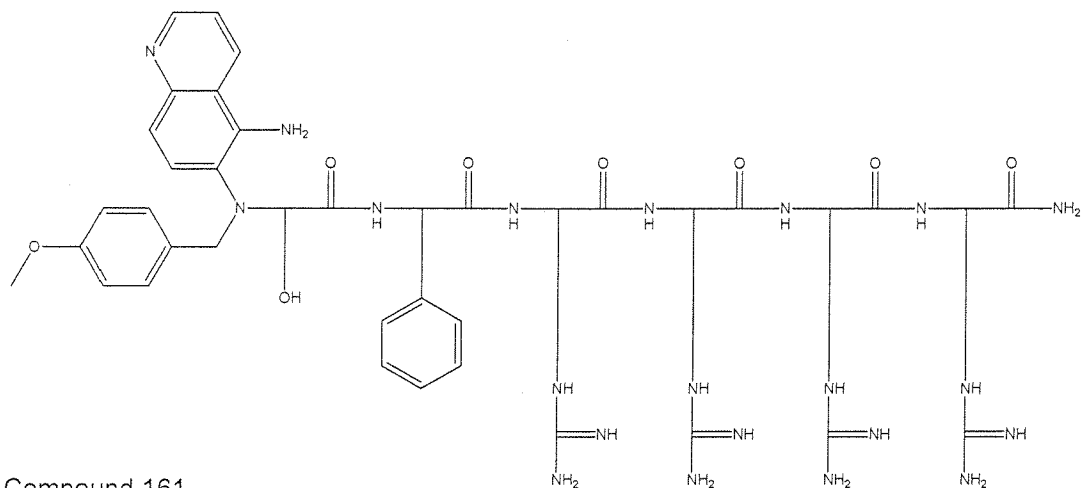


Compound 159

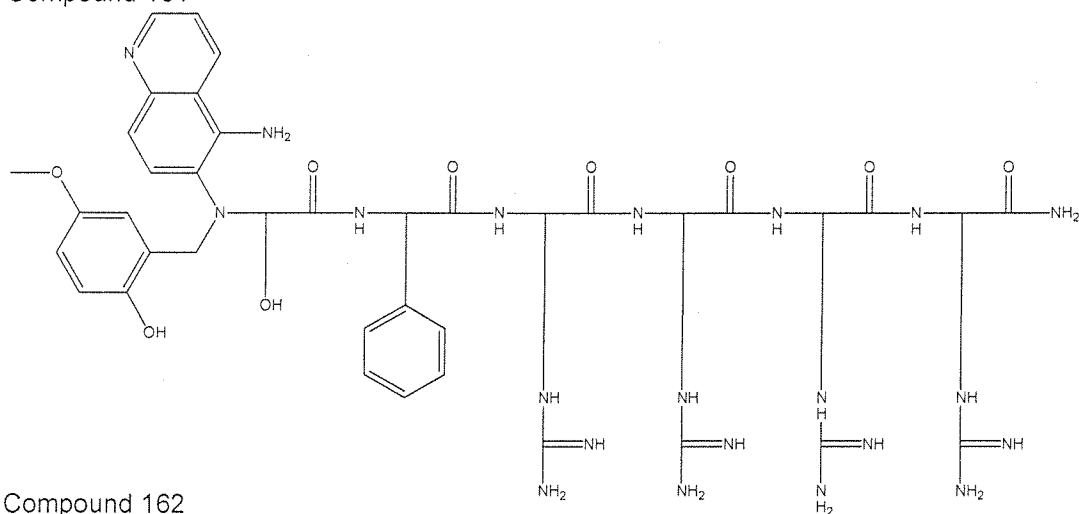


Compound 160

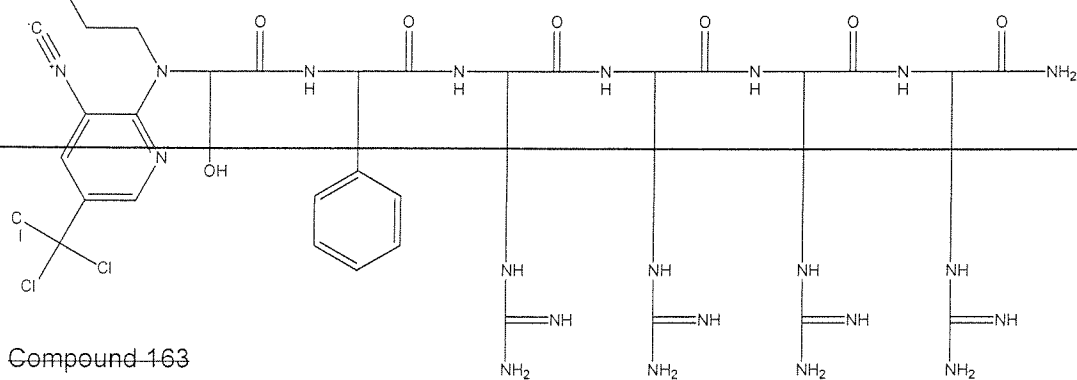
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Compound 161

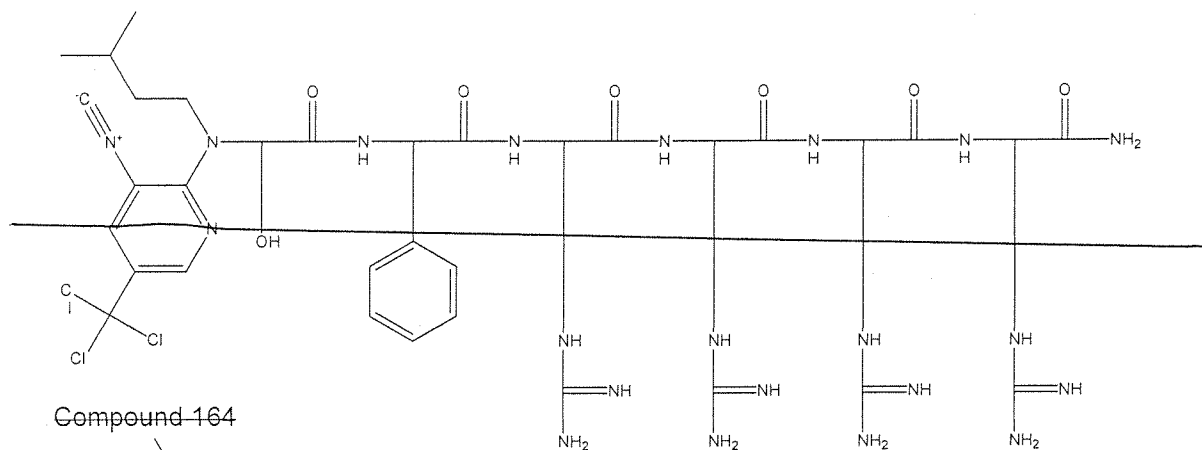


Compound 162

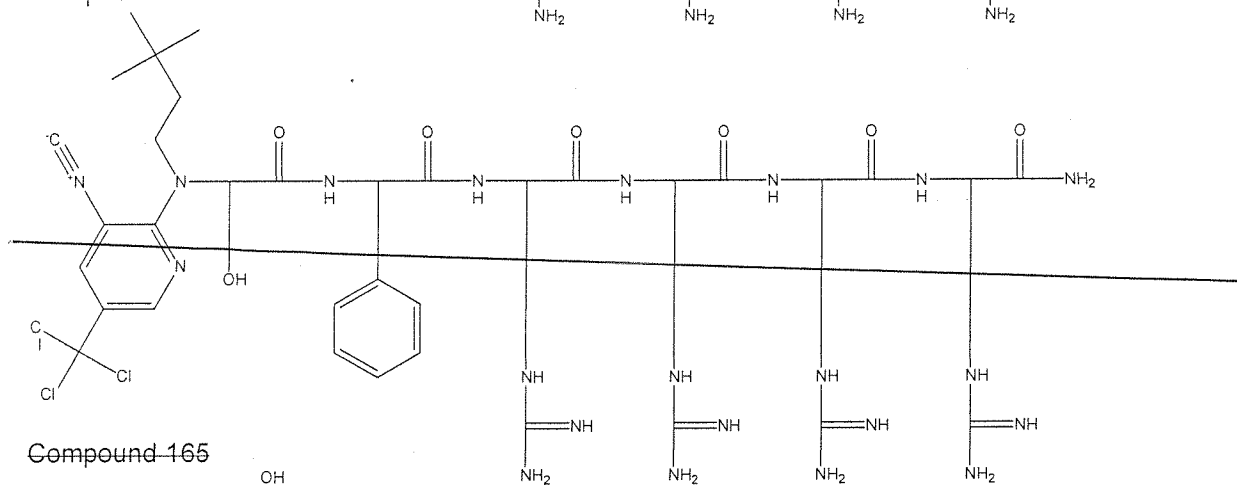


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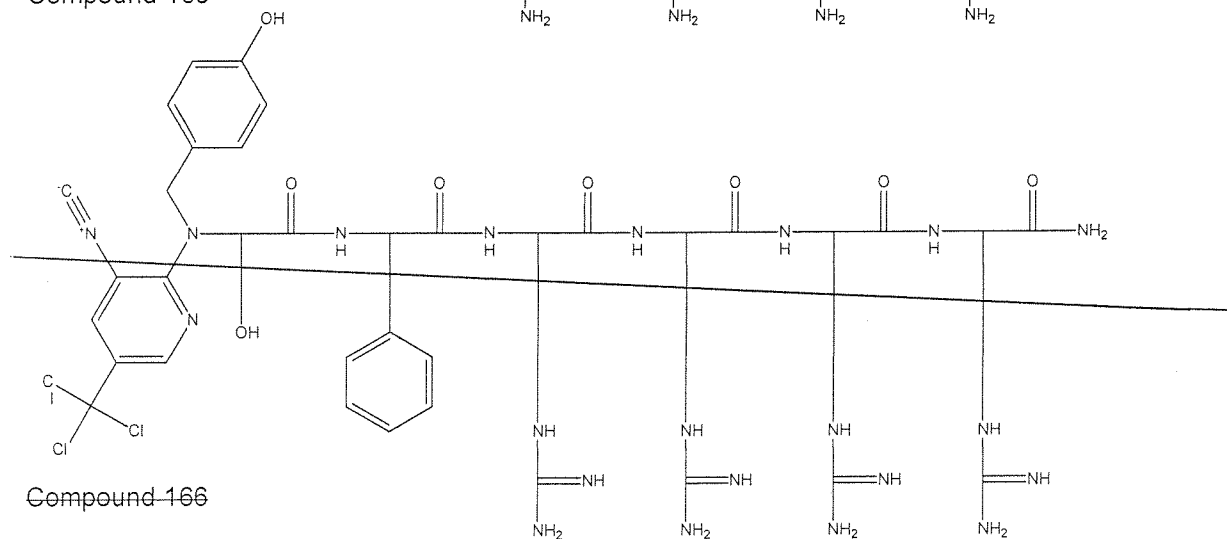
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Compound 164

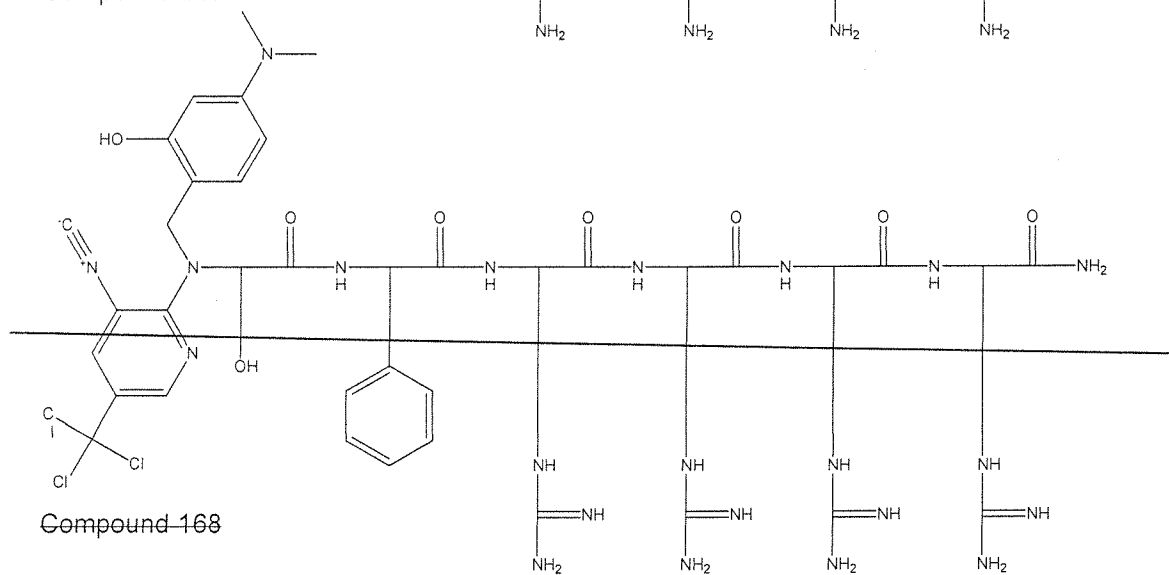
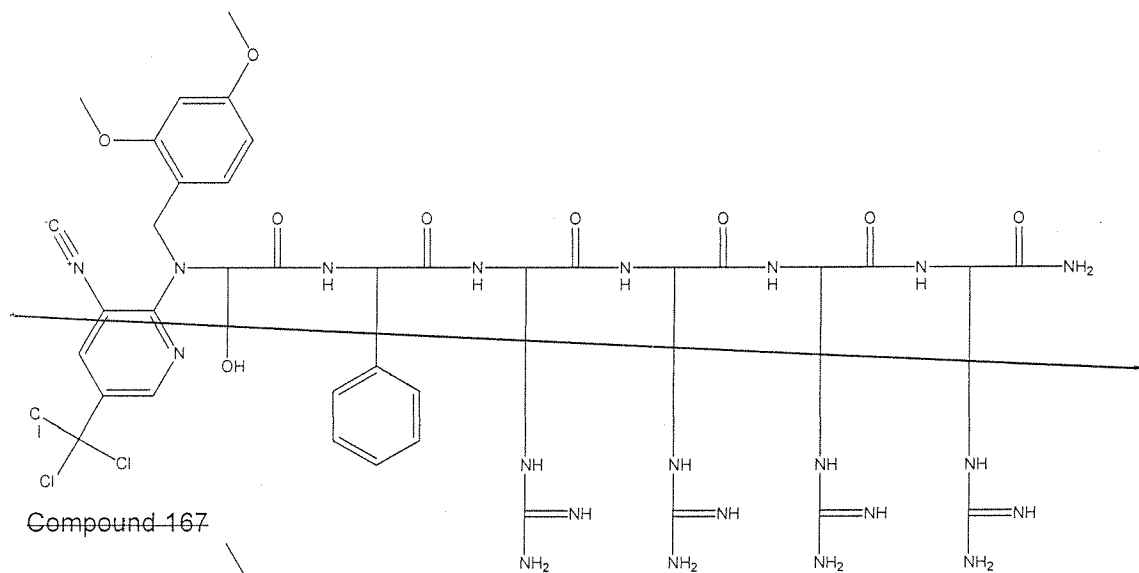


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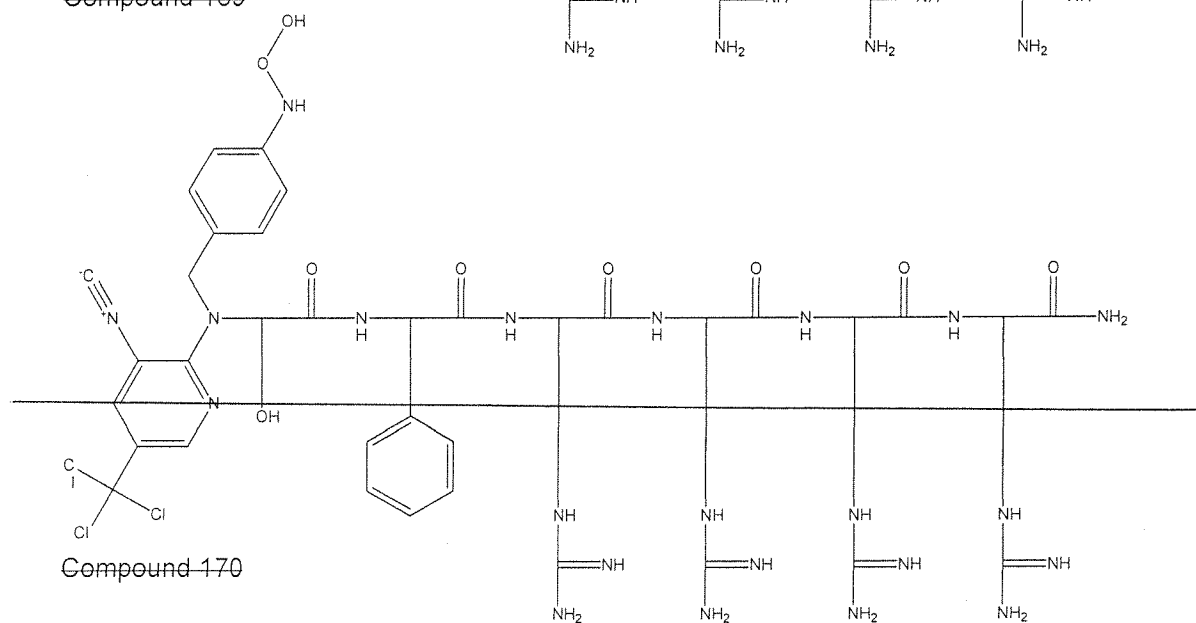
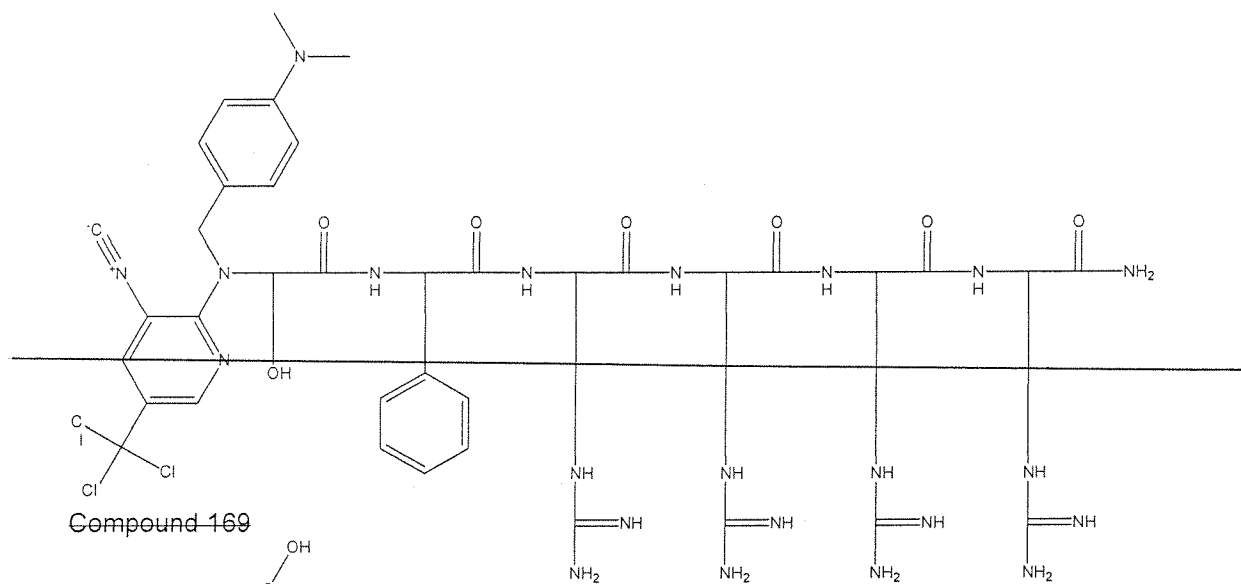


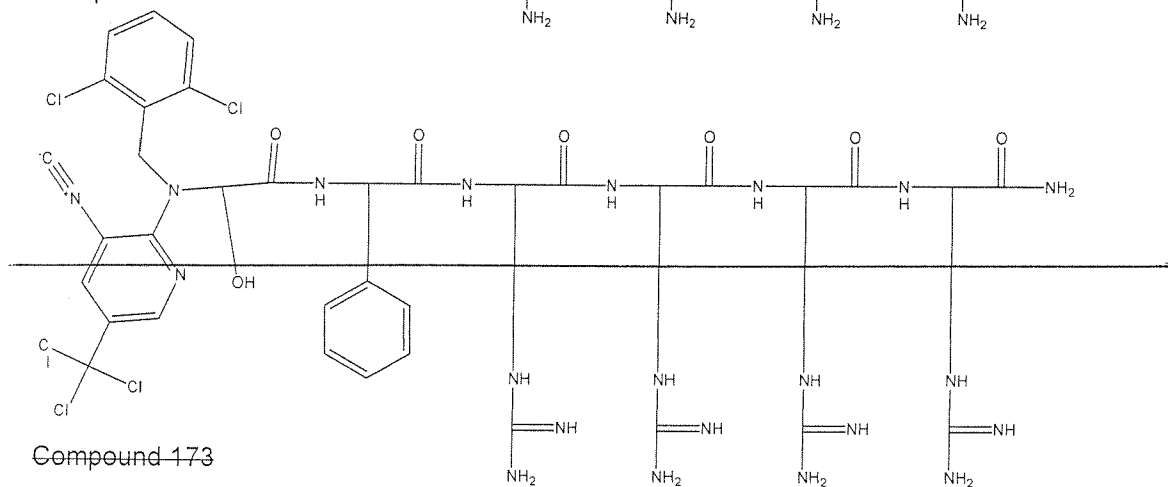
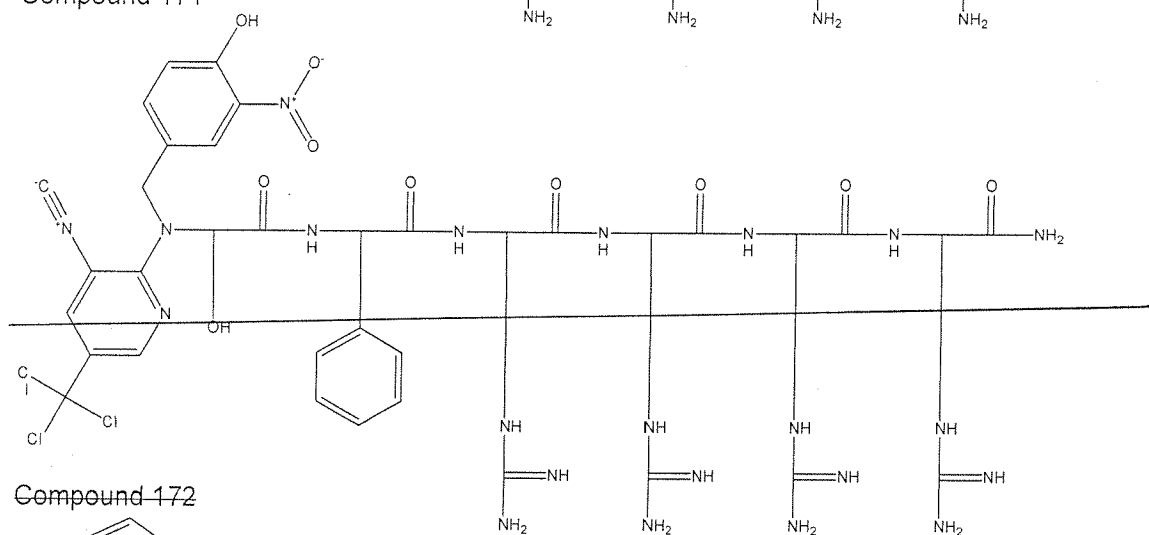
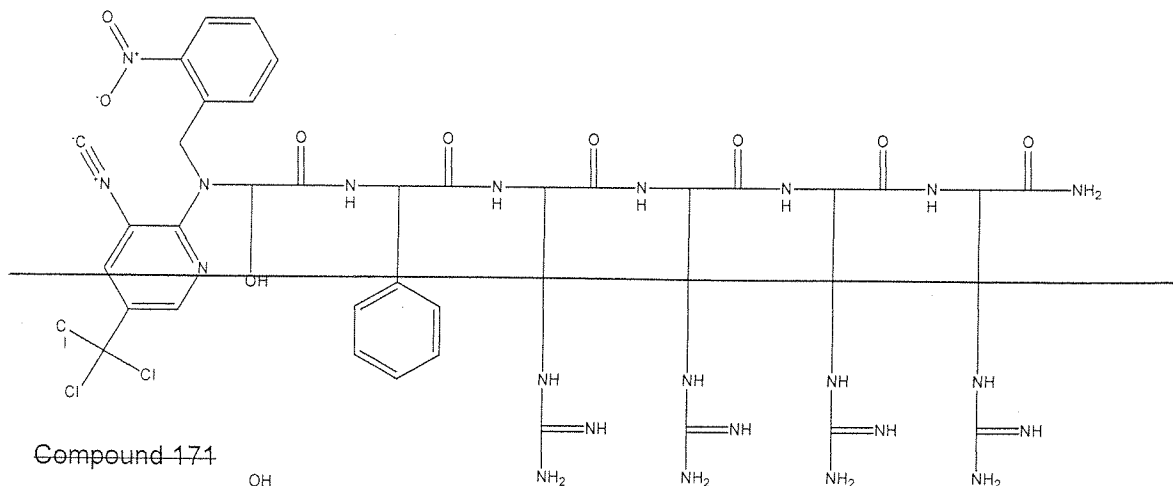
~~Compound 166~~

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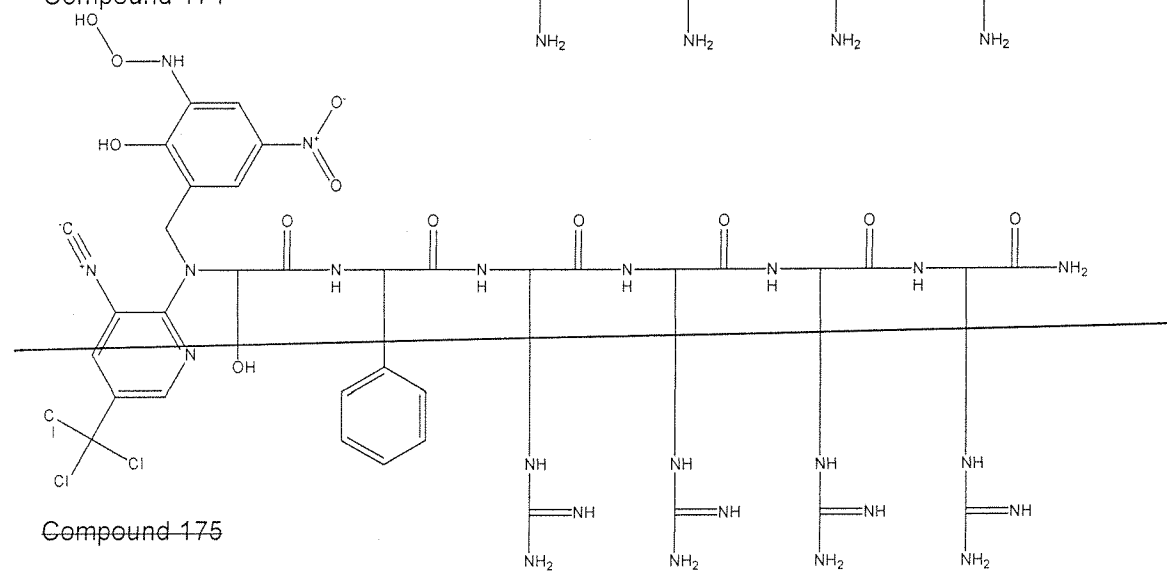
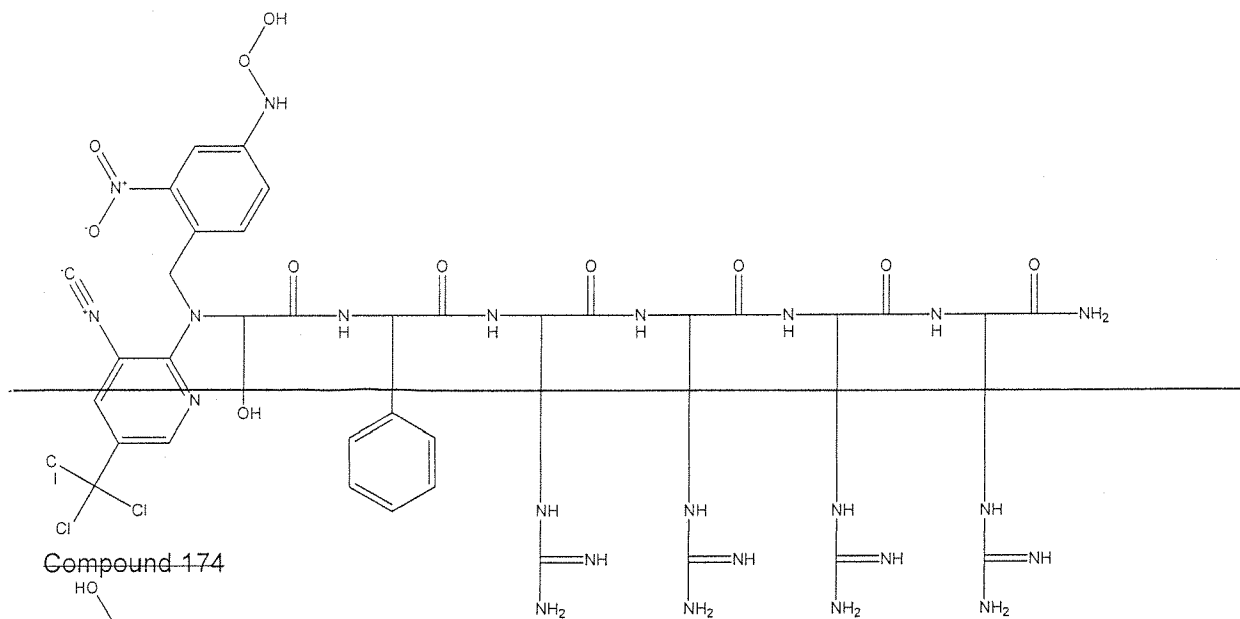


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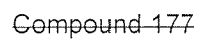
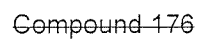




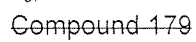
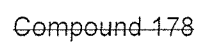
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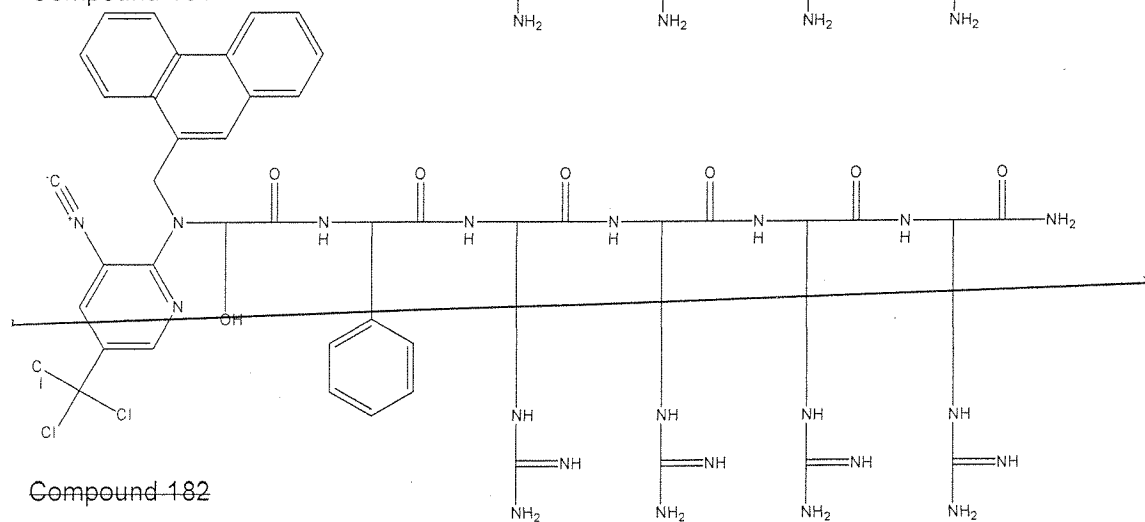
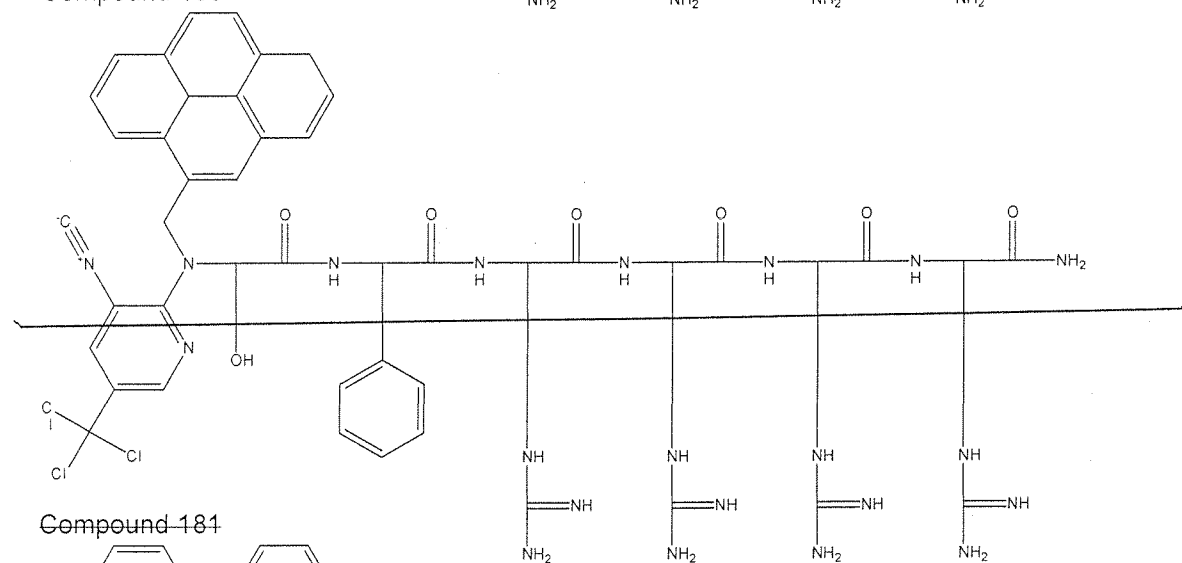
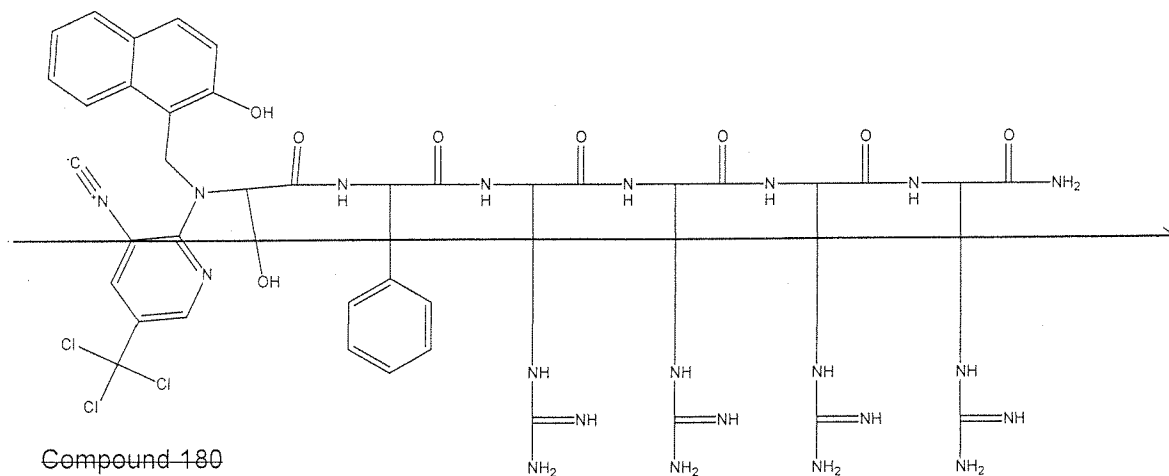


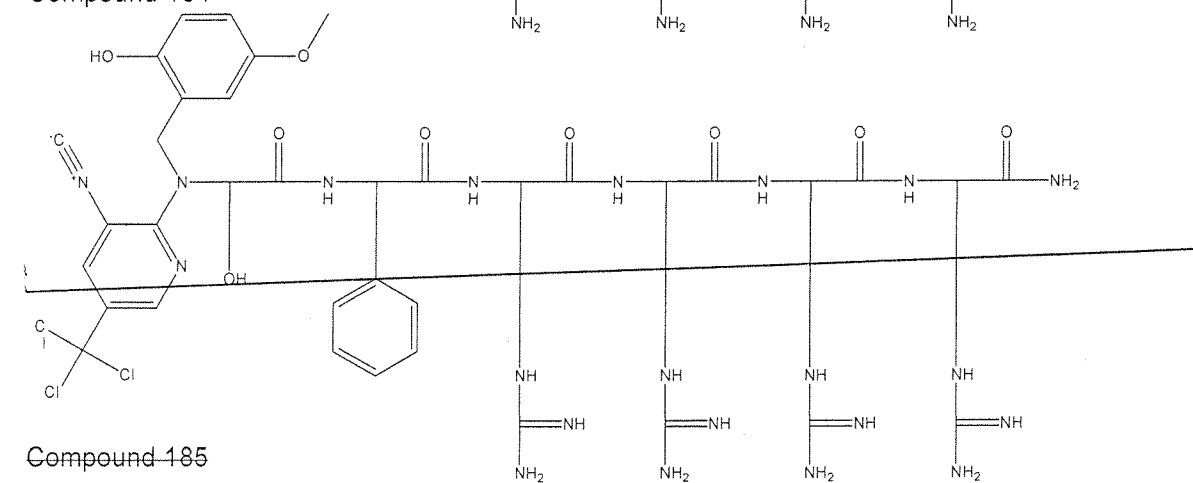
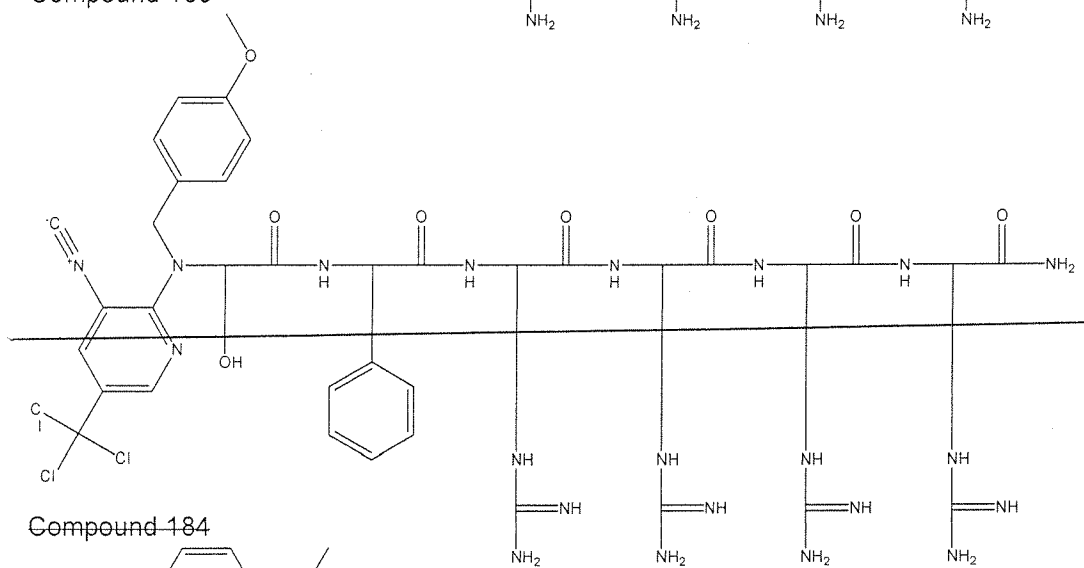
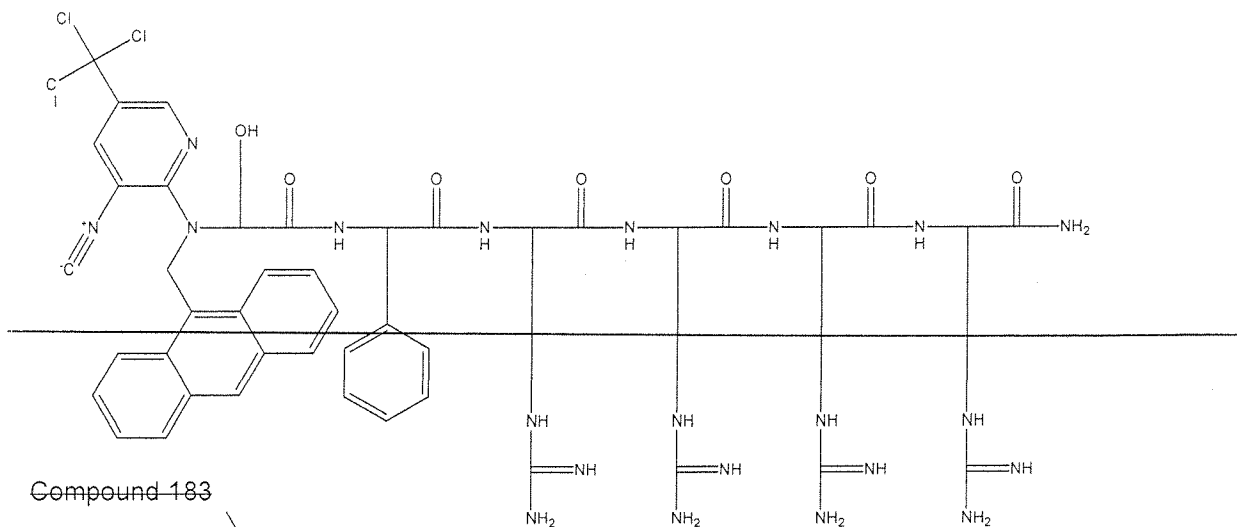
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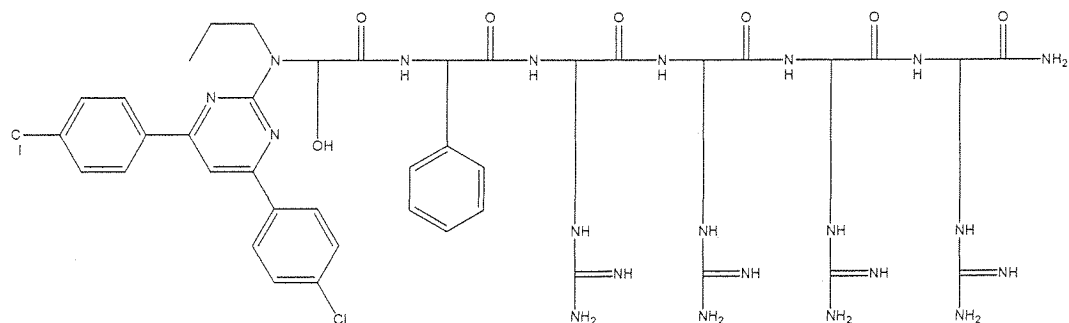
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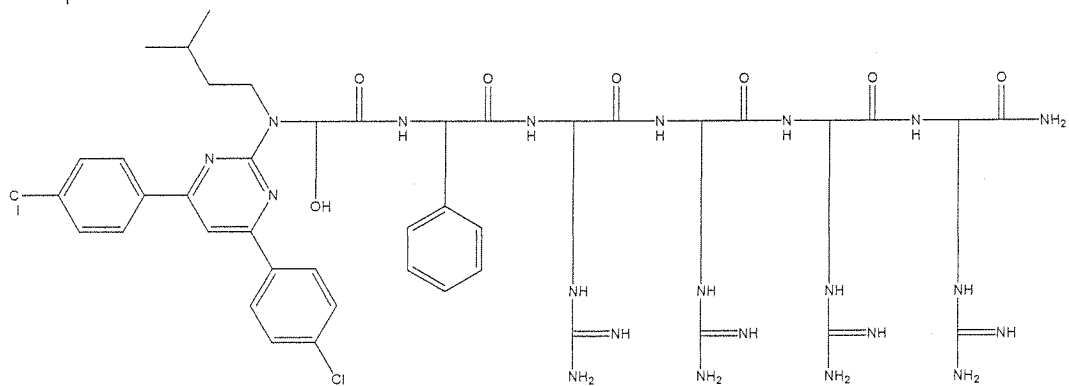




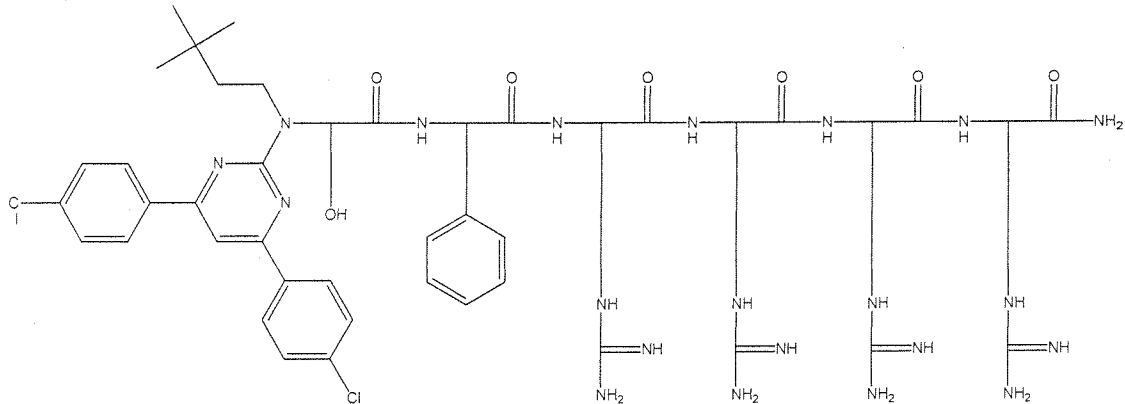
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Compound 186

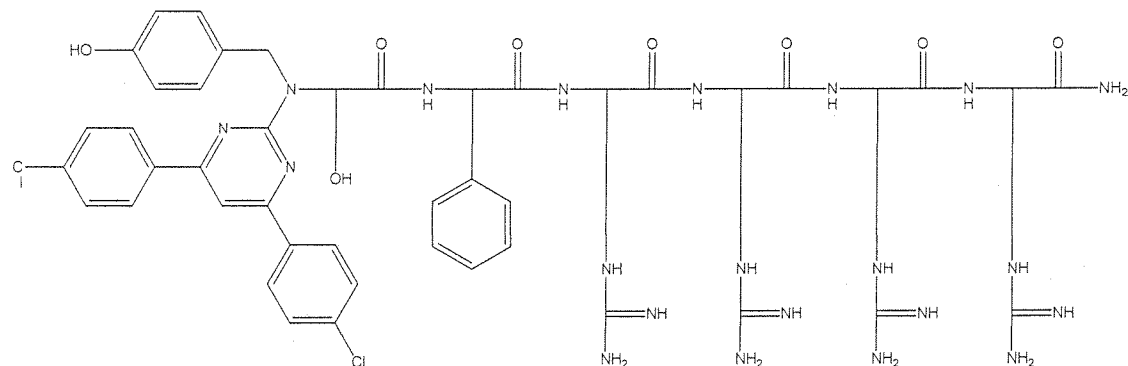


Compound 187

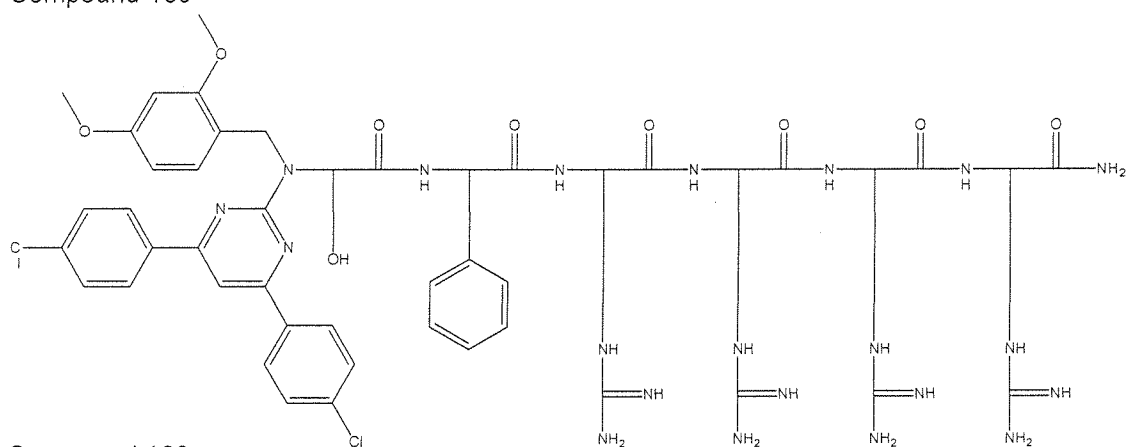


Compound 188

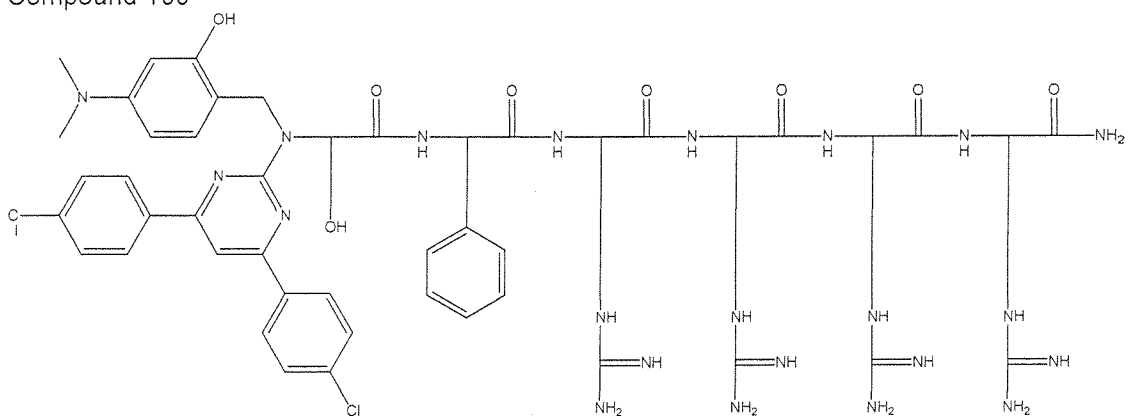
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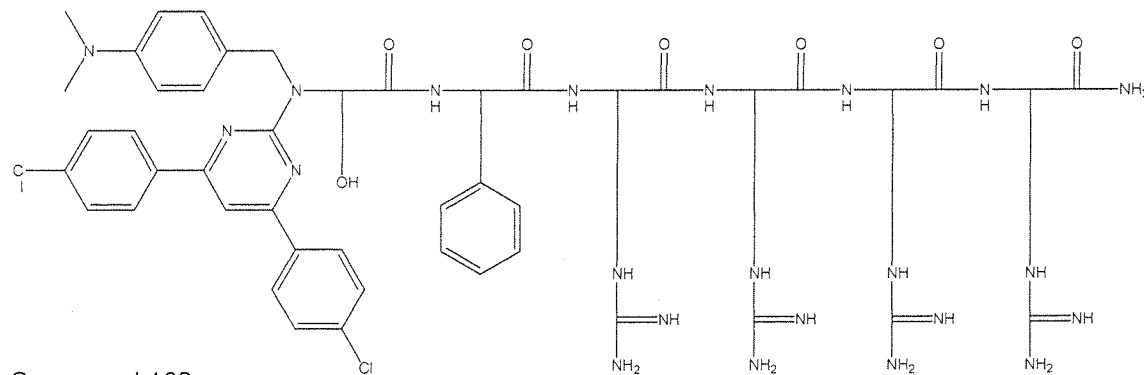
Compound 189



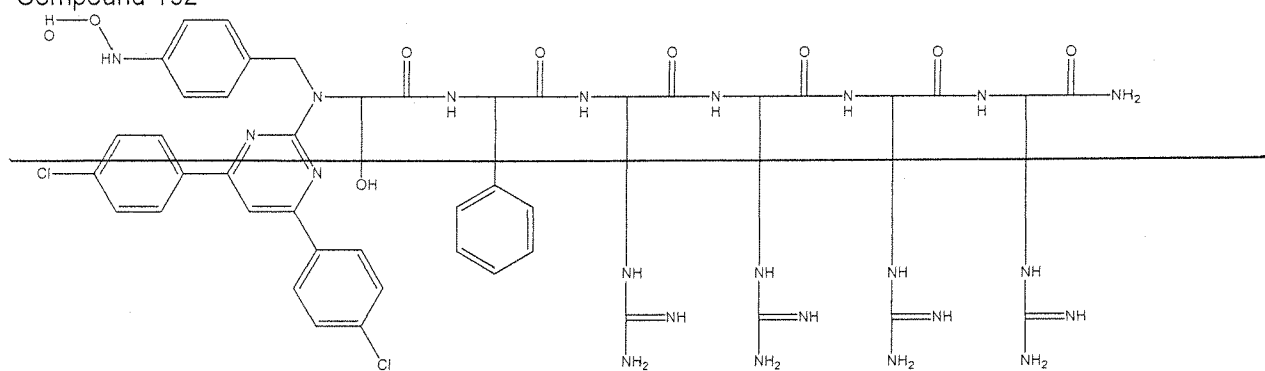
Compound 190



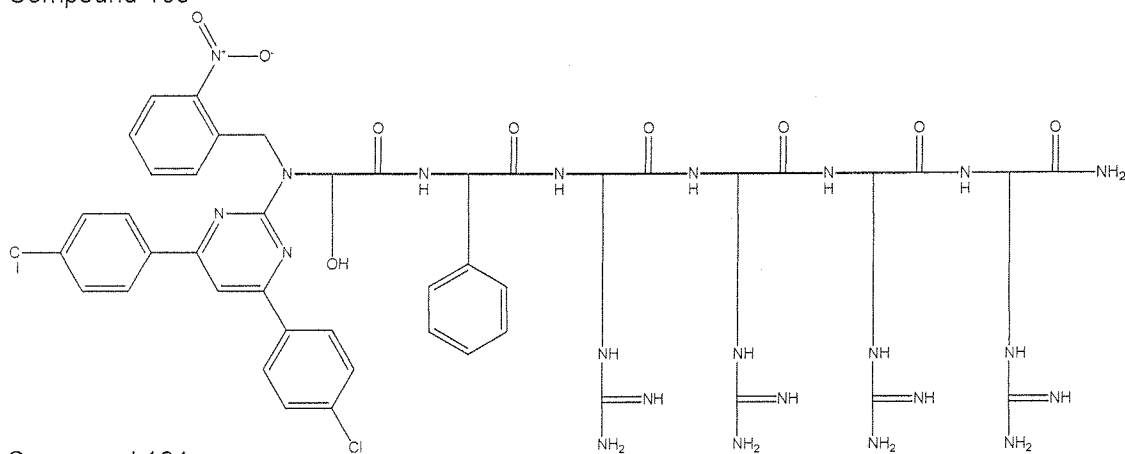
Compound 191



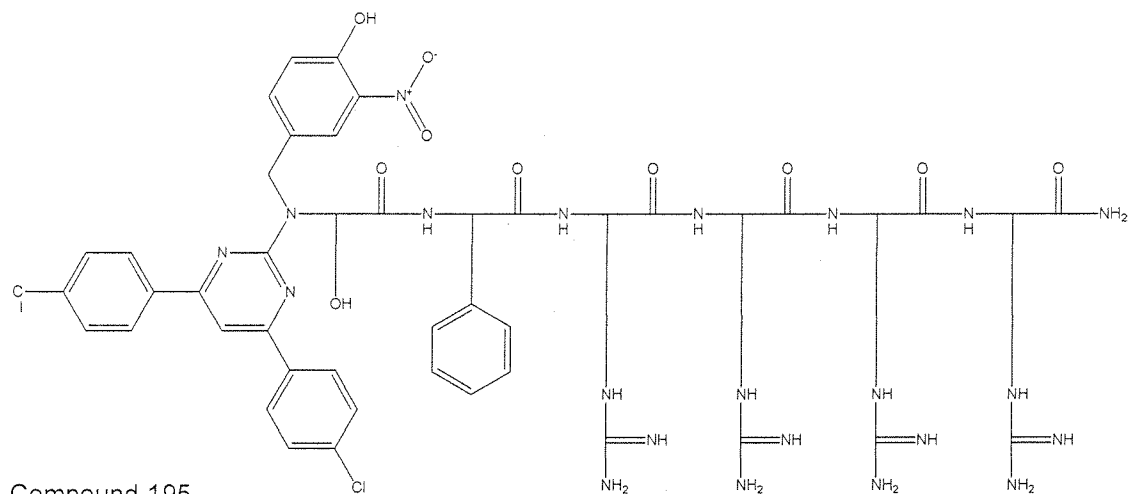
Compound 192



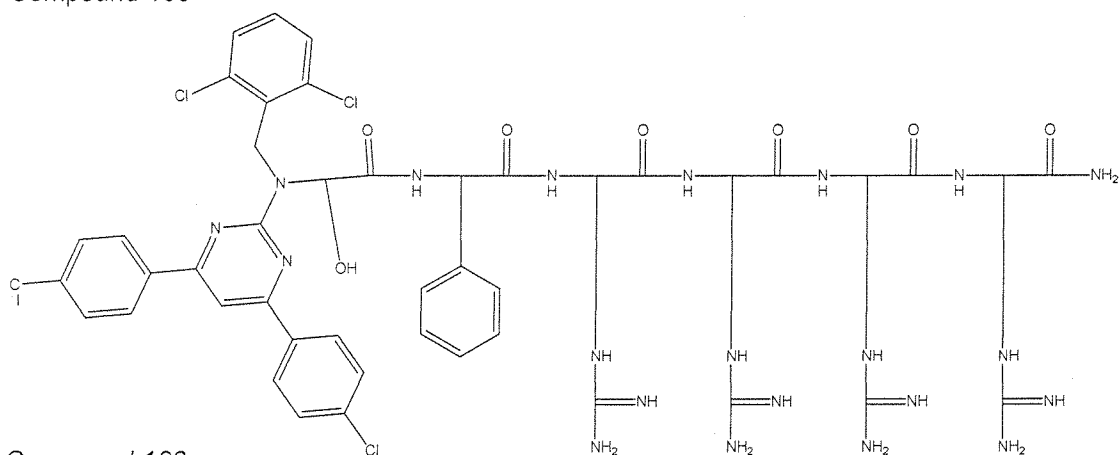
Compound 193



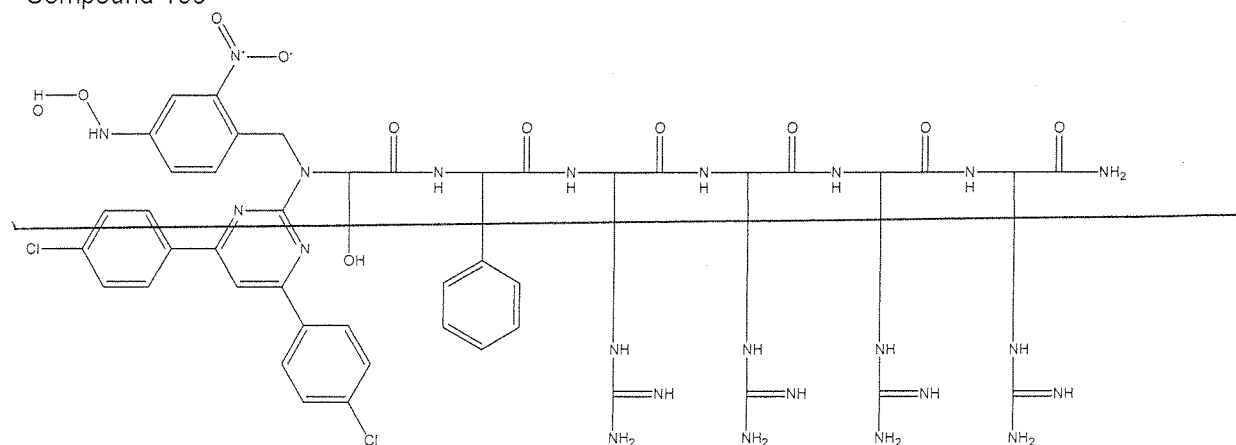
Compound 194



Compound 195

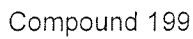
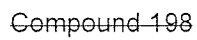


Compound 196

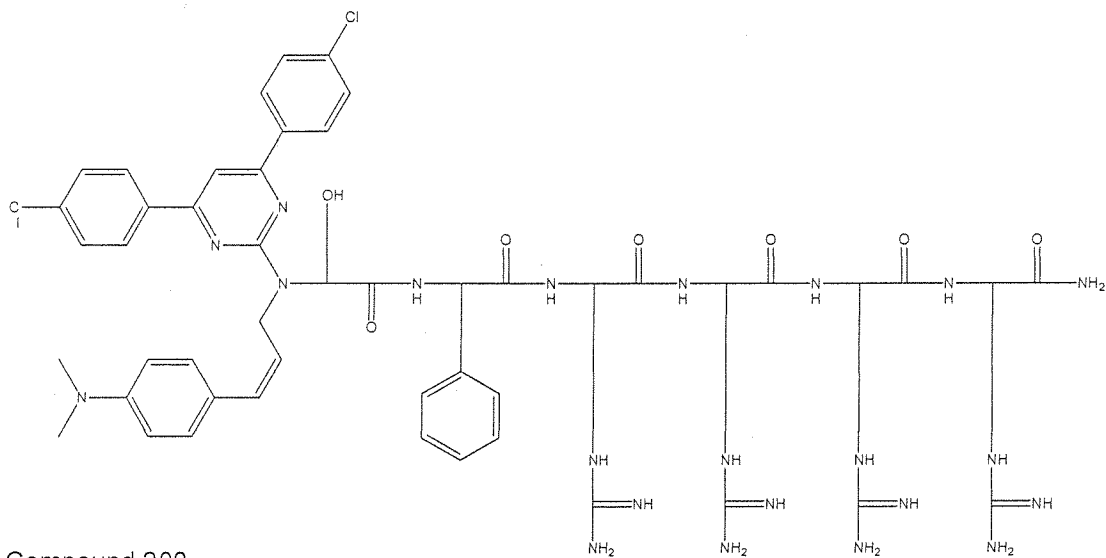


Compound 197

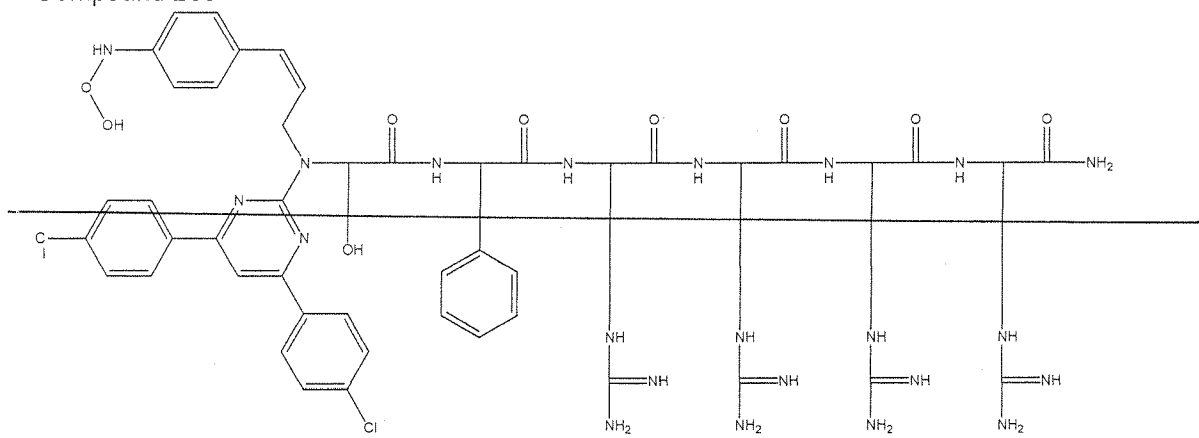
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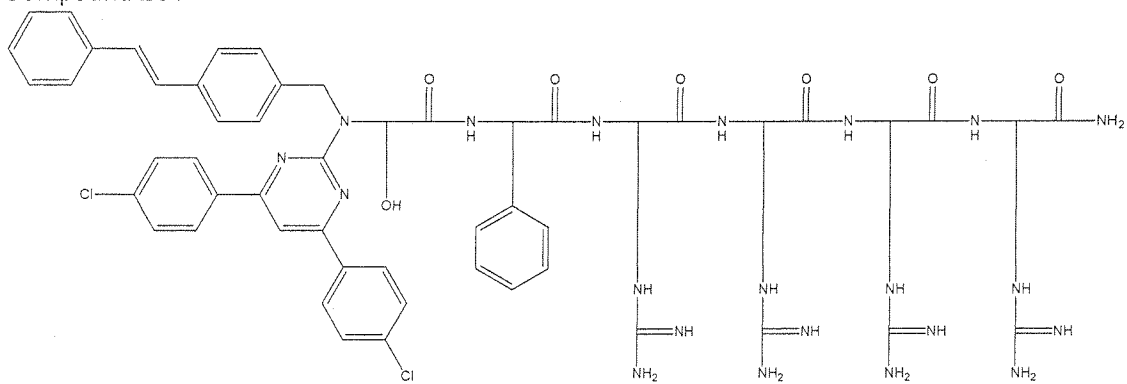
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Compound 200

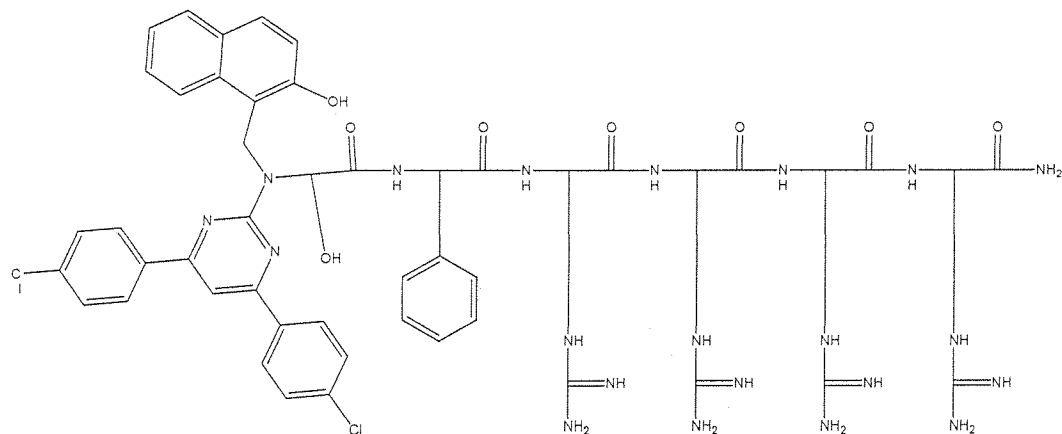


~~Compound 201~~

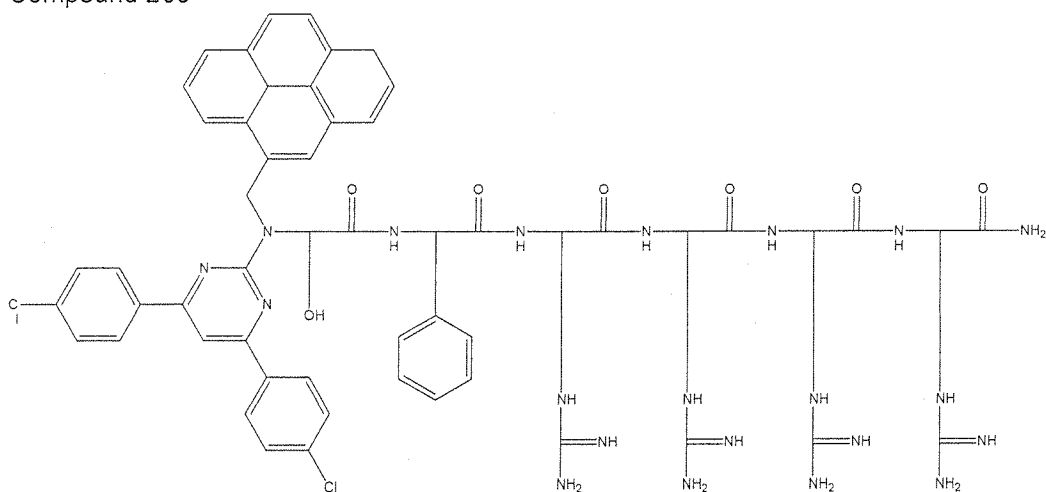


Compound 202

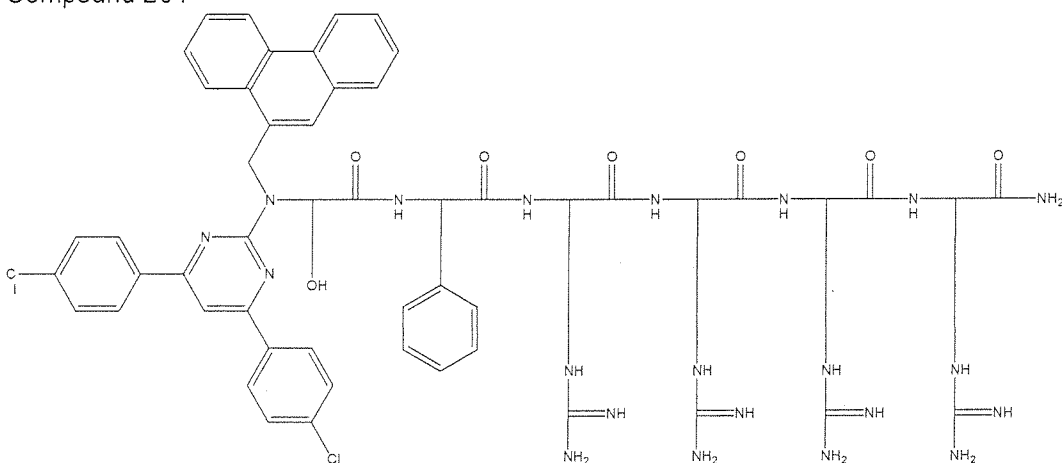
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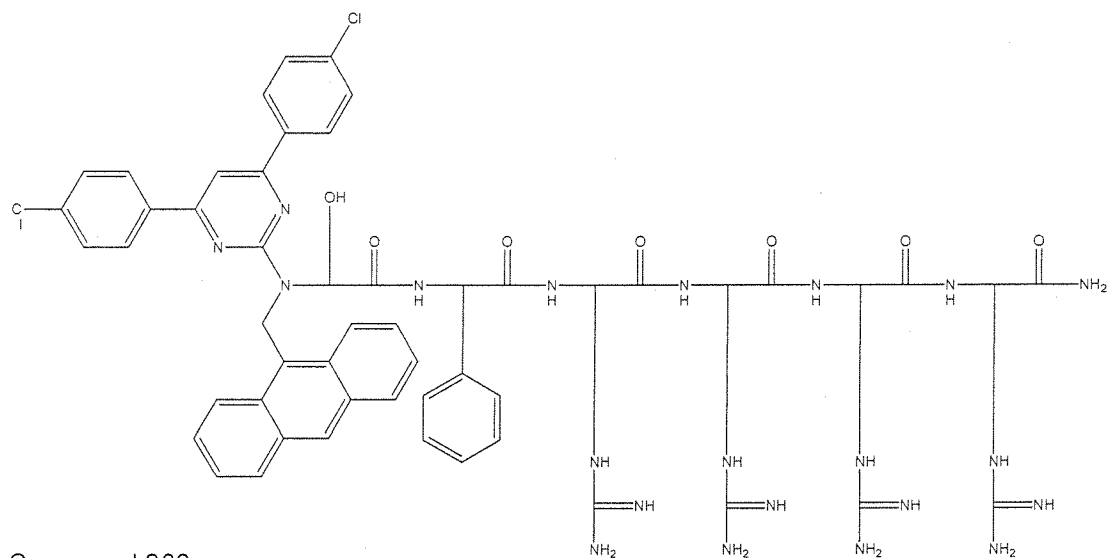
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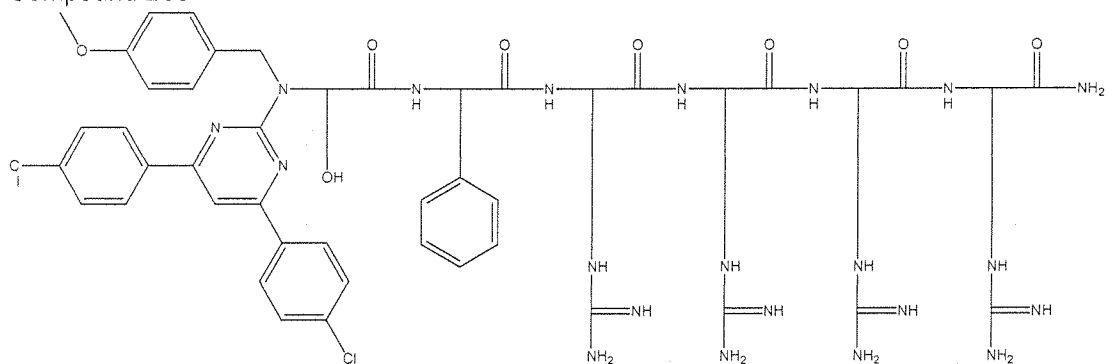
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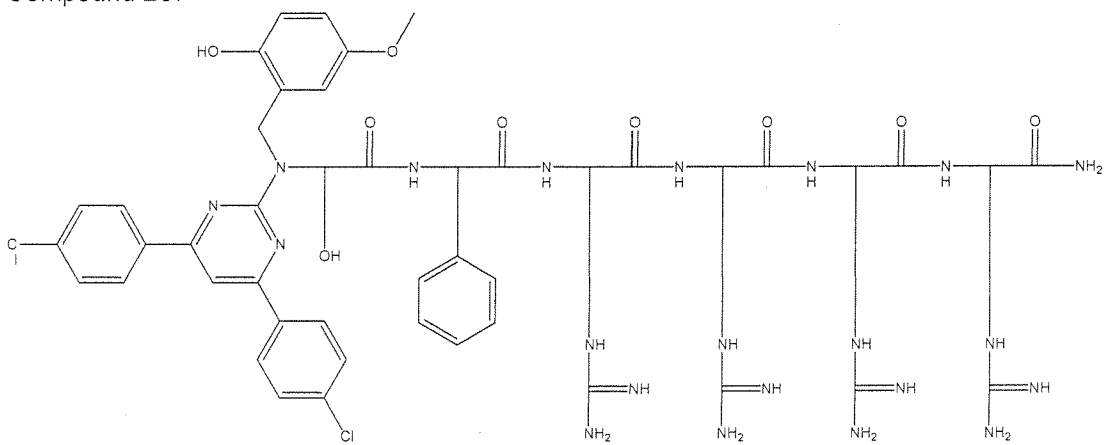
Compound 205



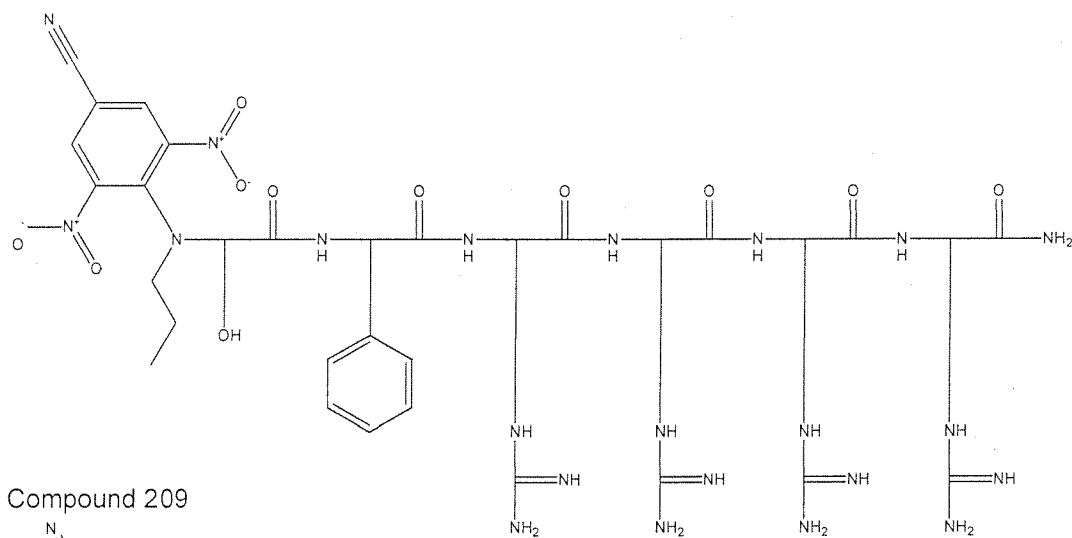
Compound 206



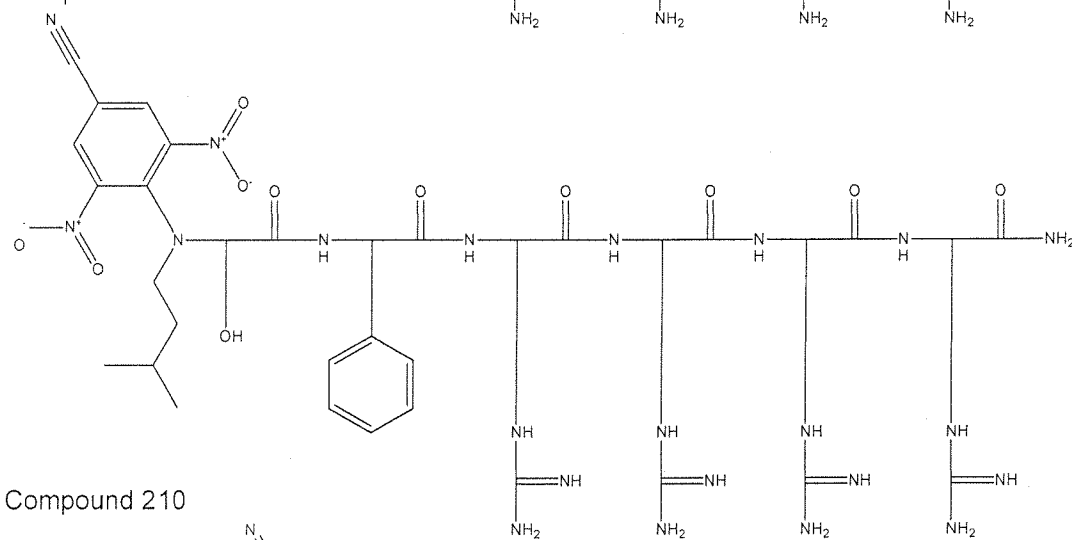
Compound 207



Compound 208

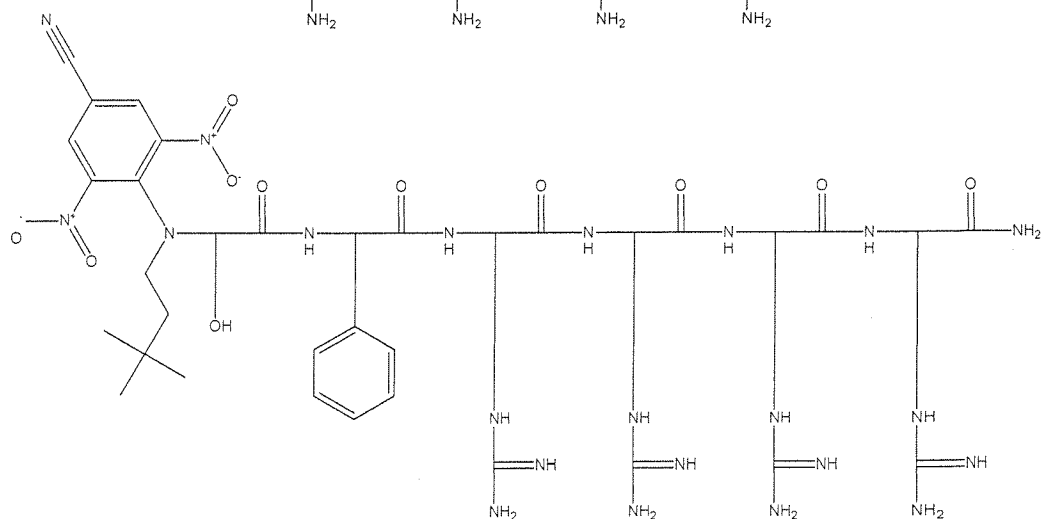


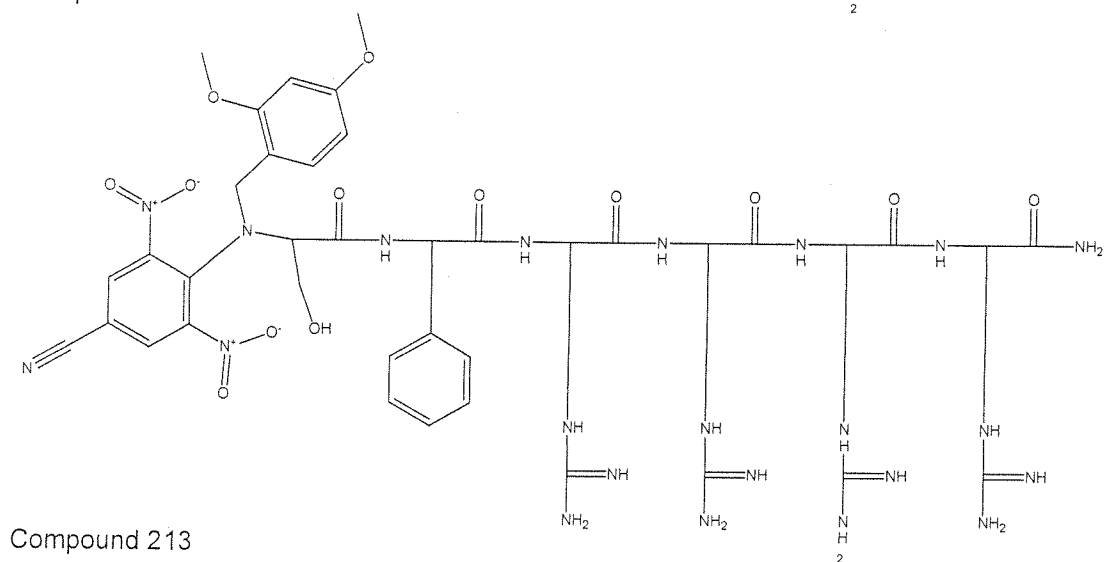
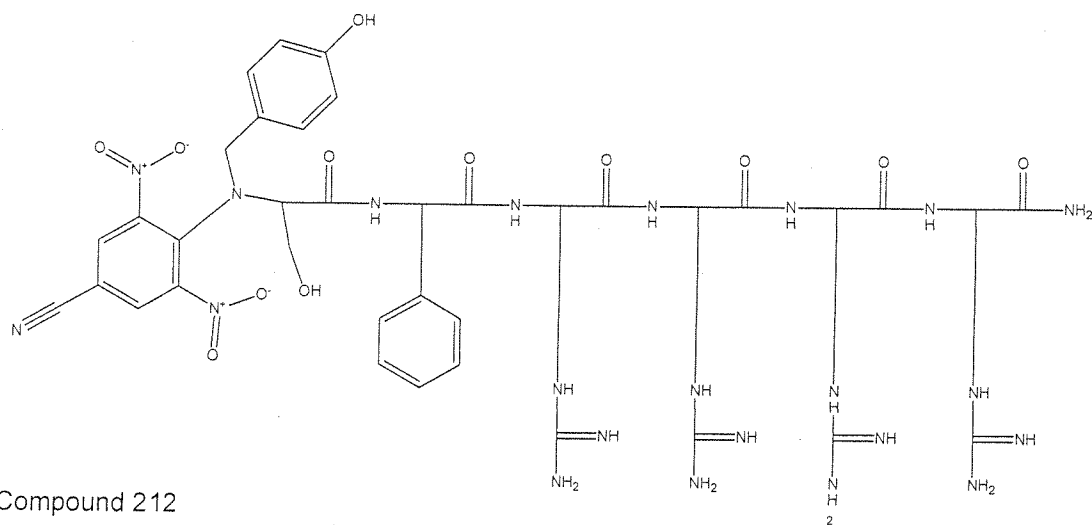
Compound 209



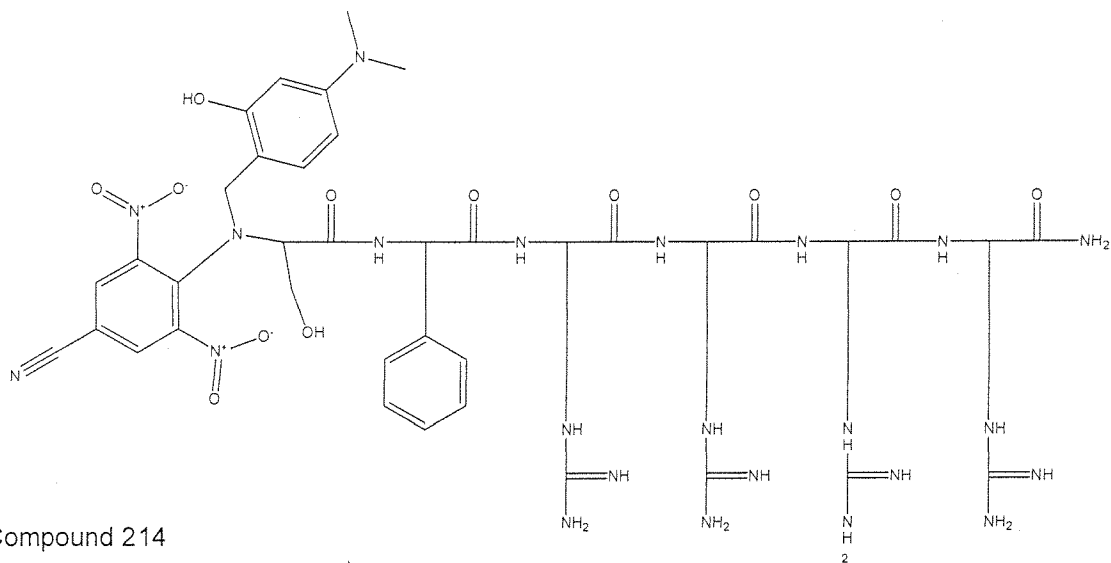
Compound 210

Compound 211

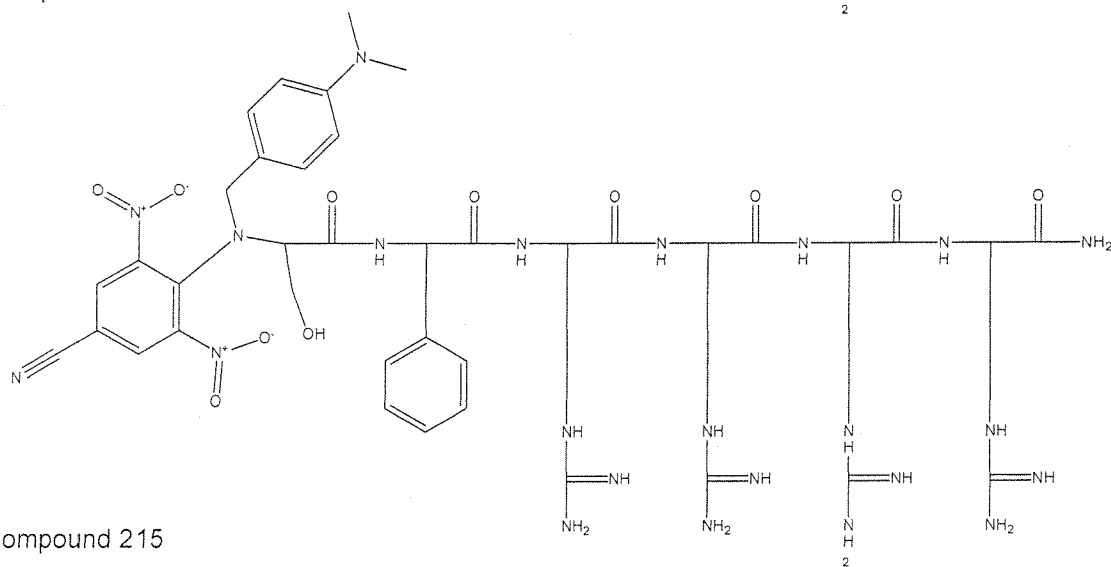




446510.1

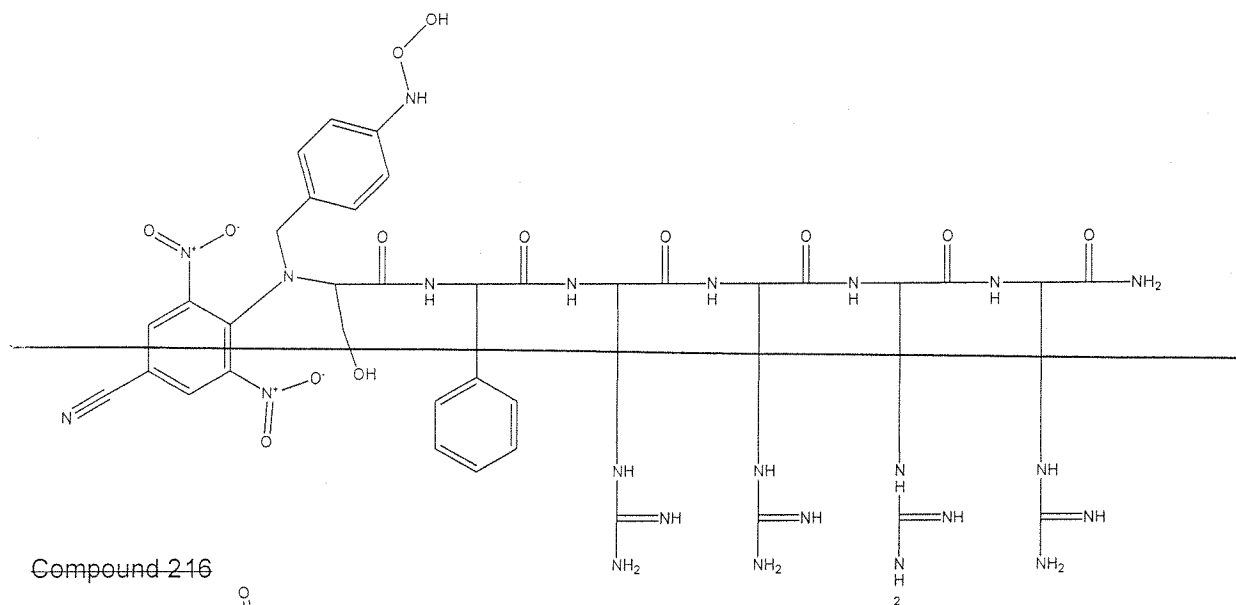


Compound 214

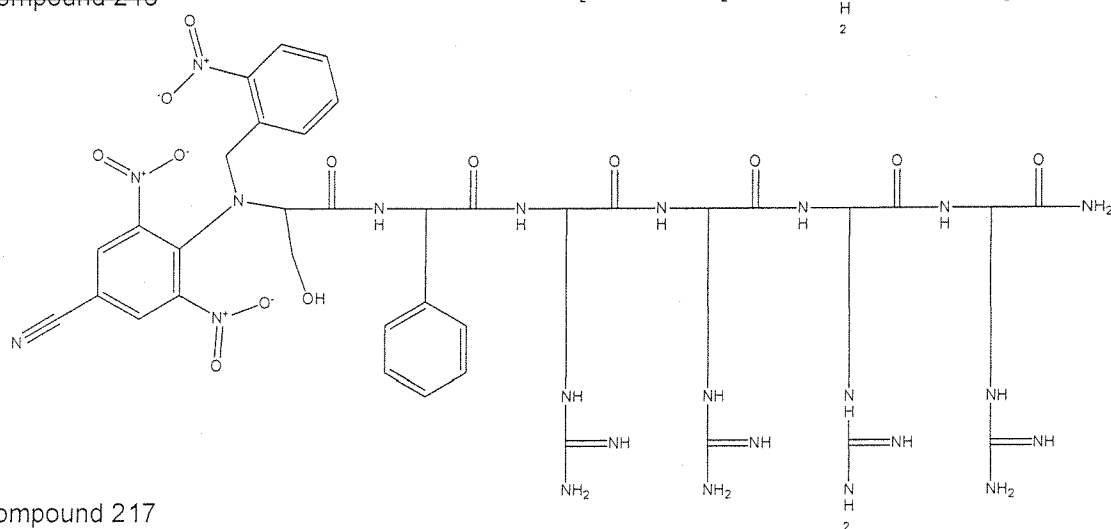


Compound 215

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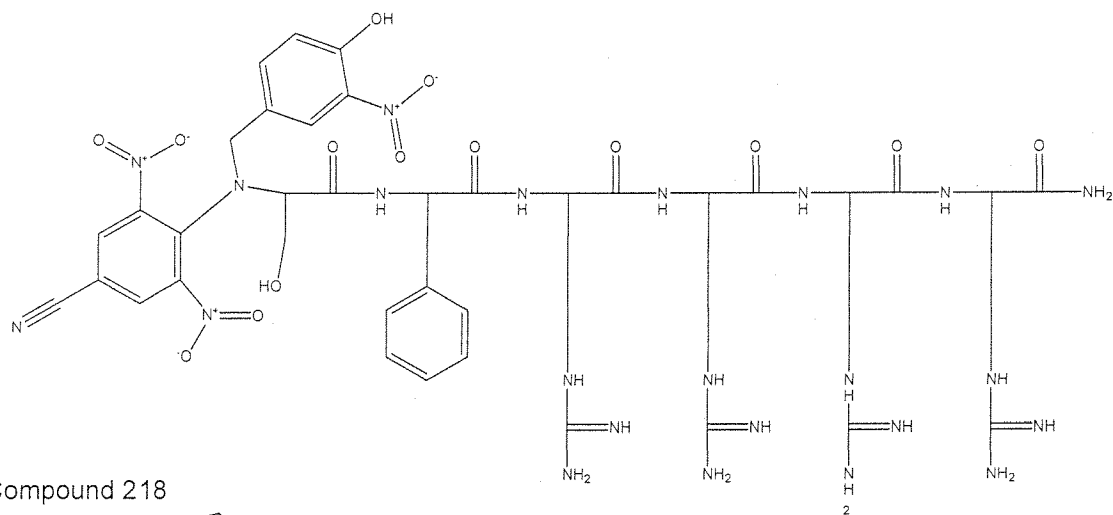


Compound 216

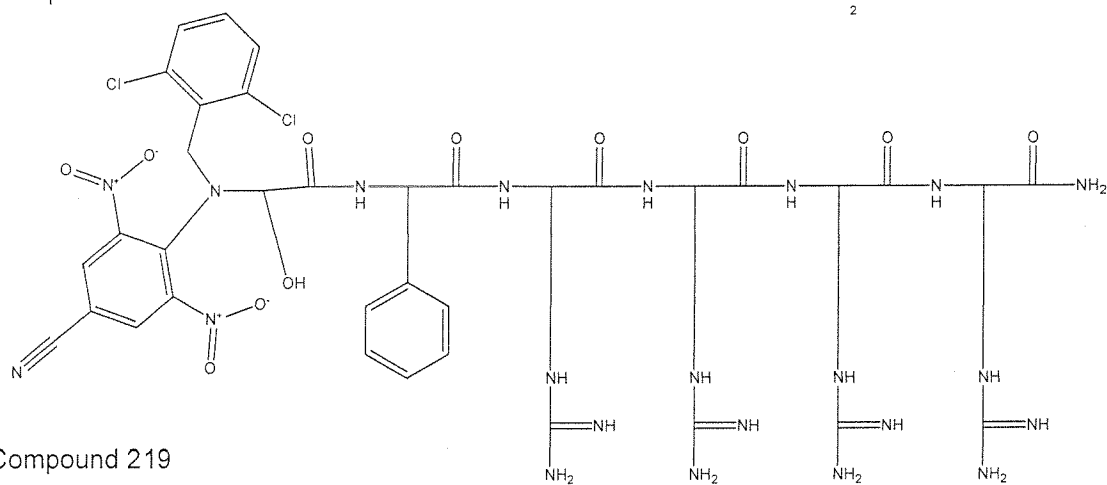


Compound 217

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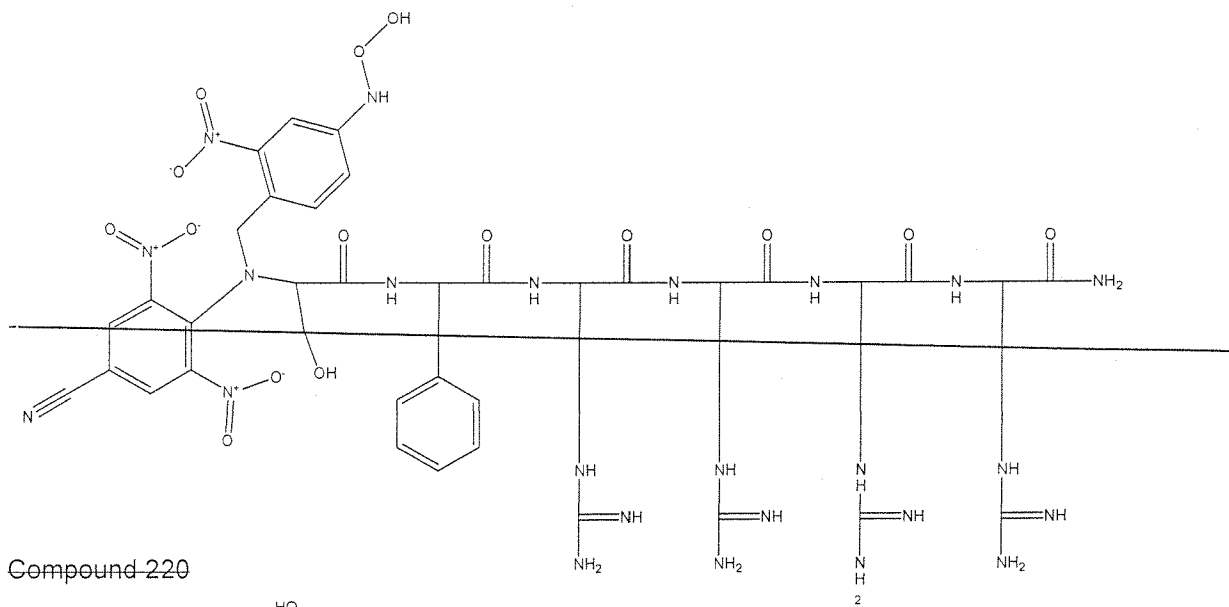


Compound 218

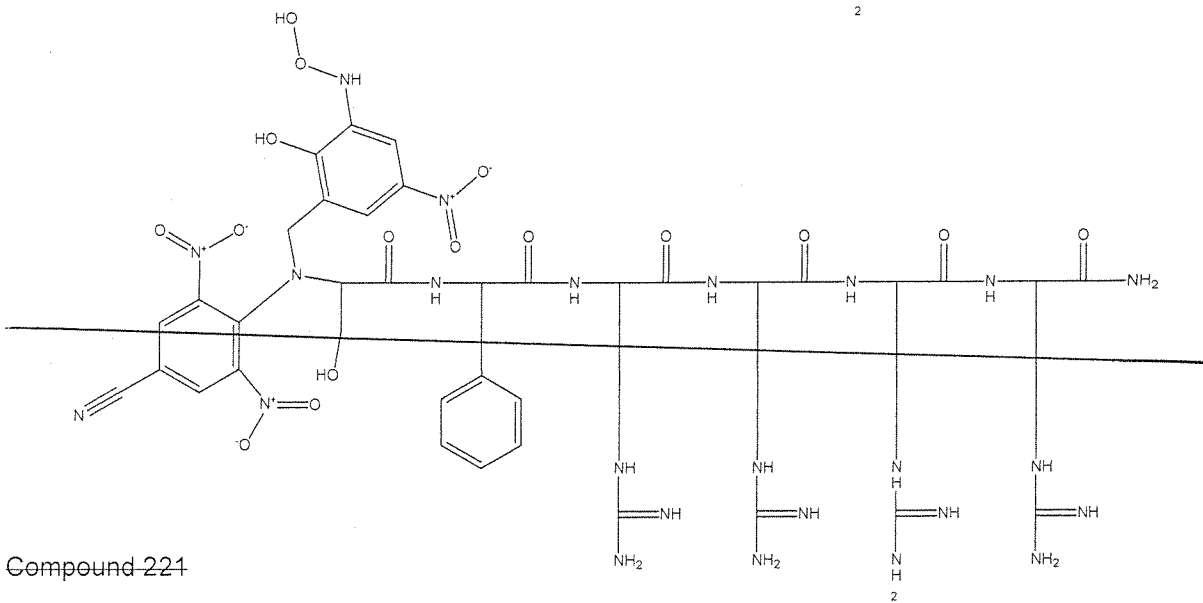


Compound 219

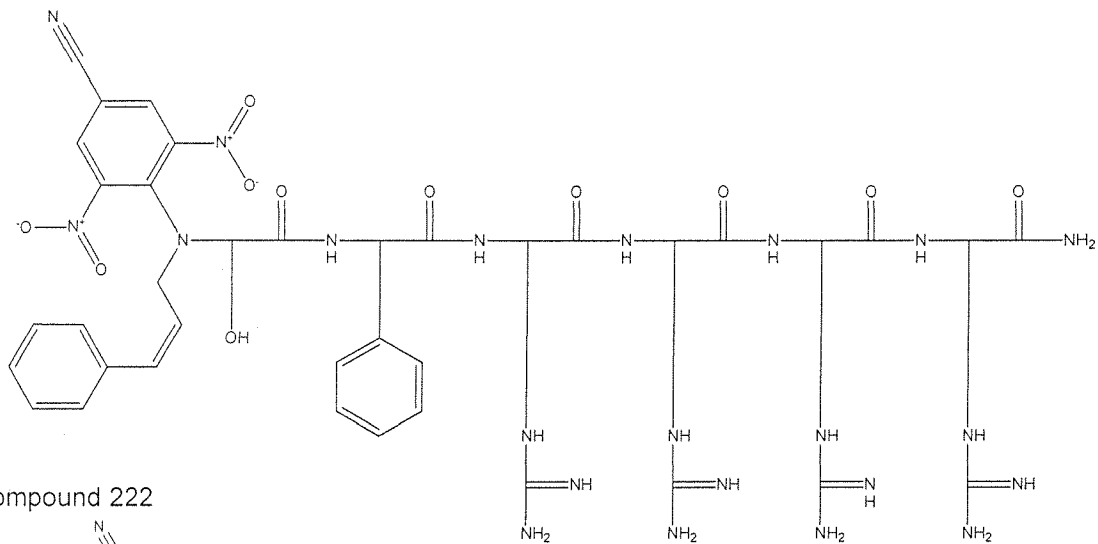
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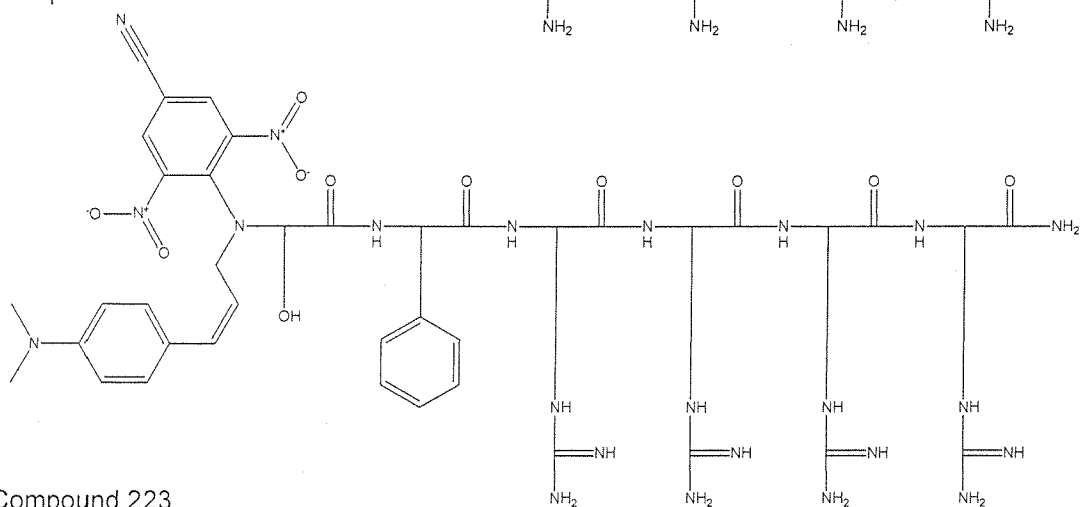
~~Compound 220~~



~~Compound 221~~

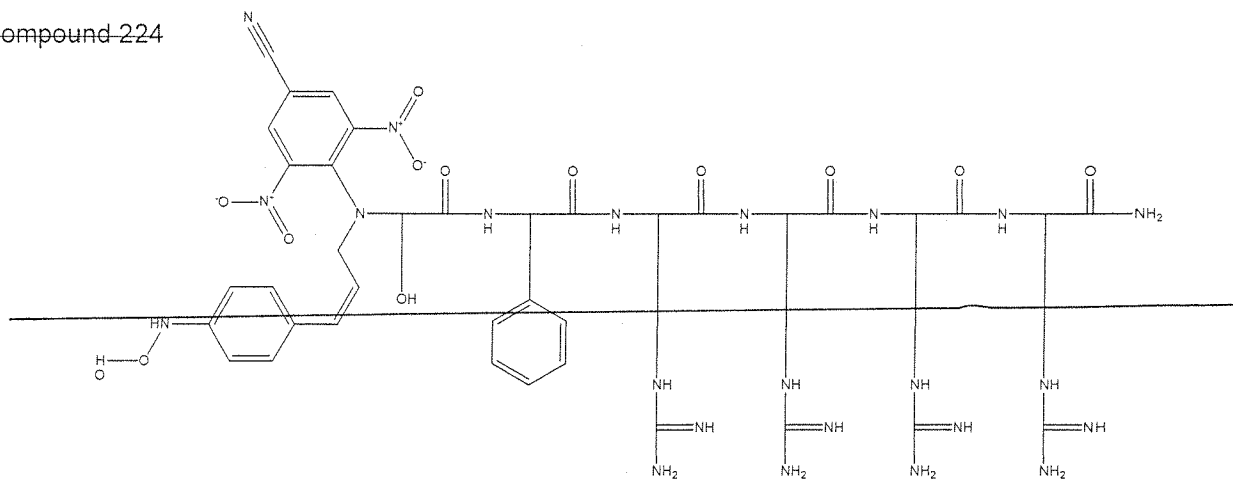


Compound 222

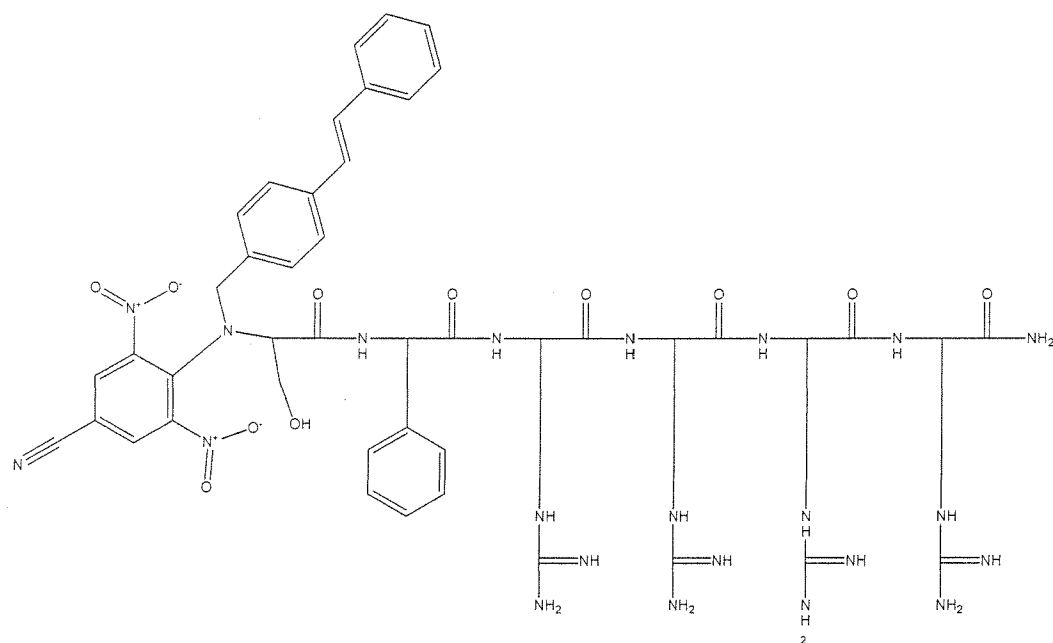


Compound 223

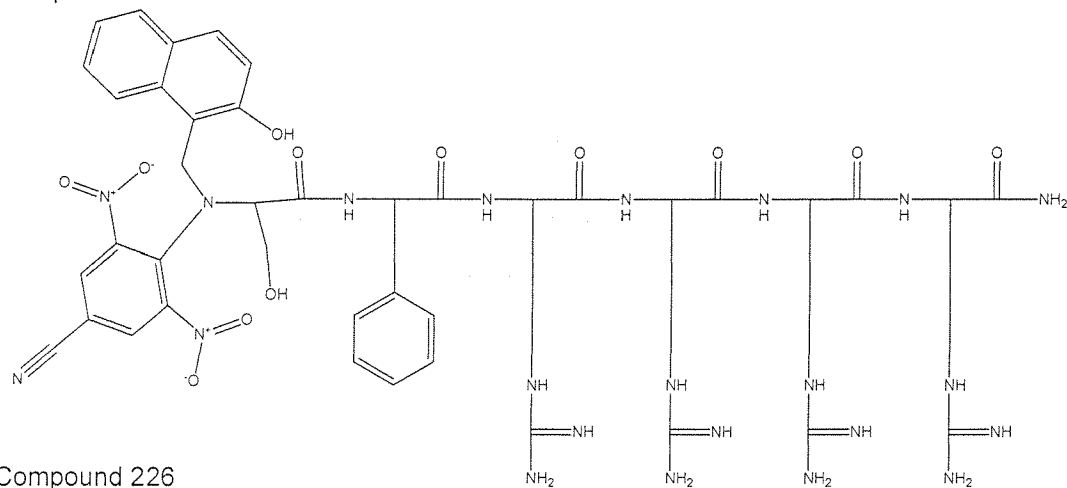
Compound 224



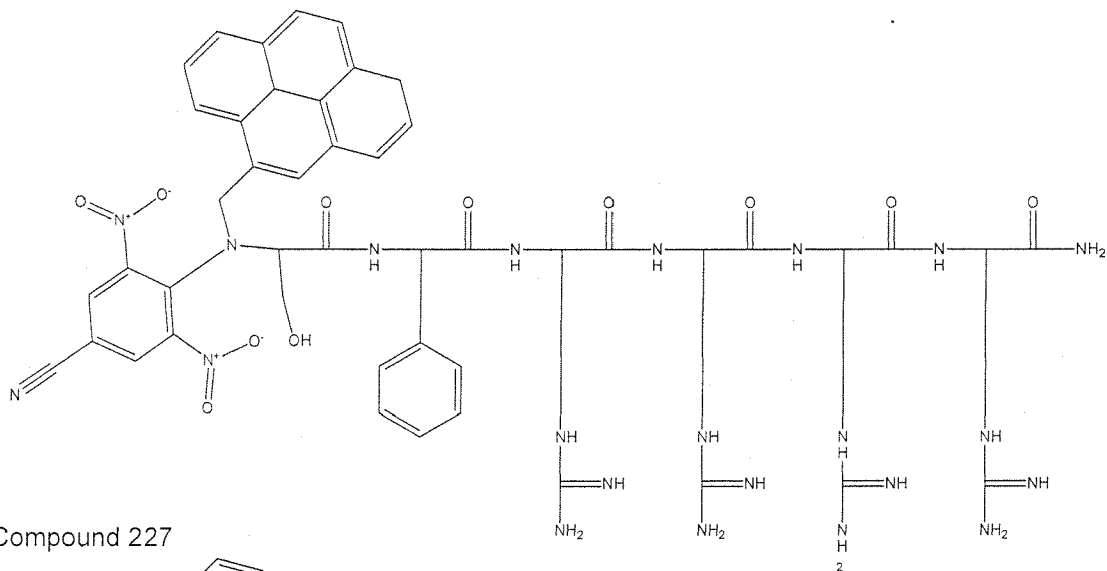
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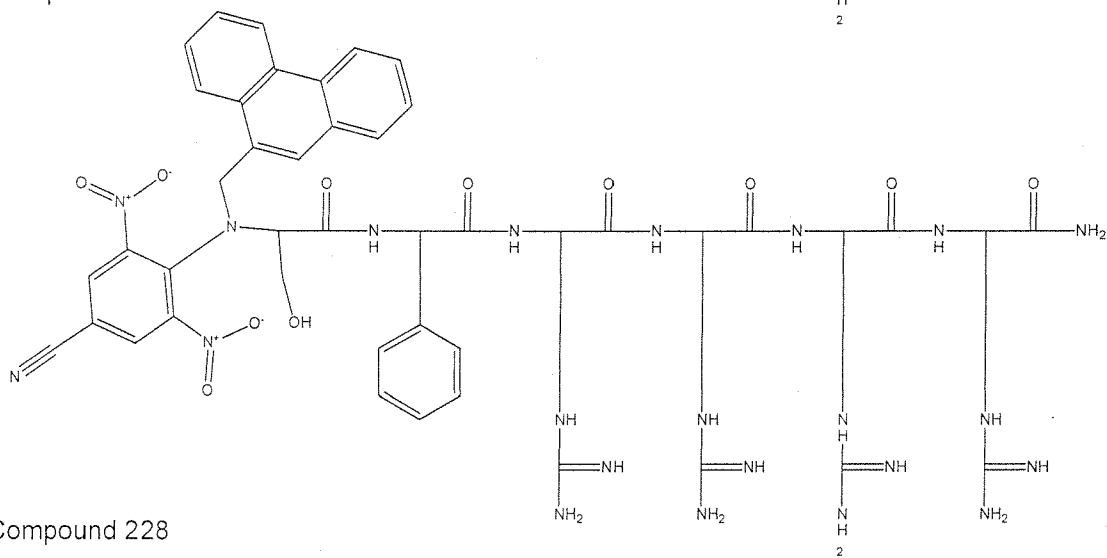
Compound 225



Compound 226

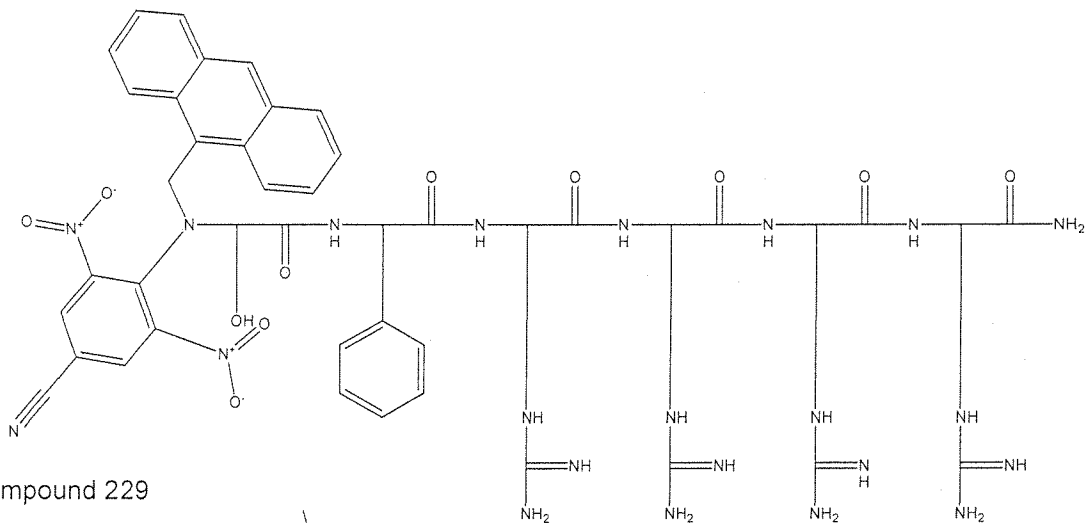


Compound 227

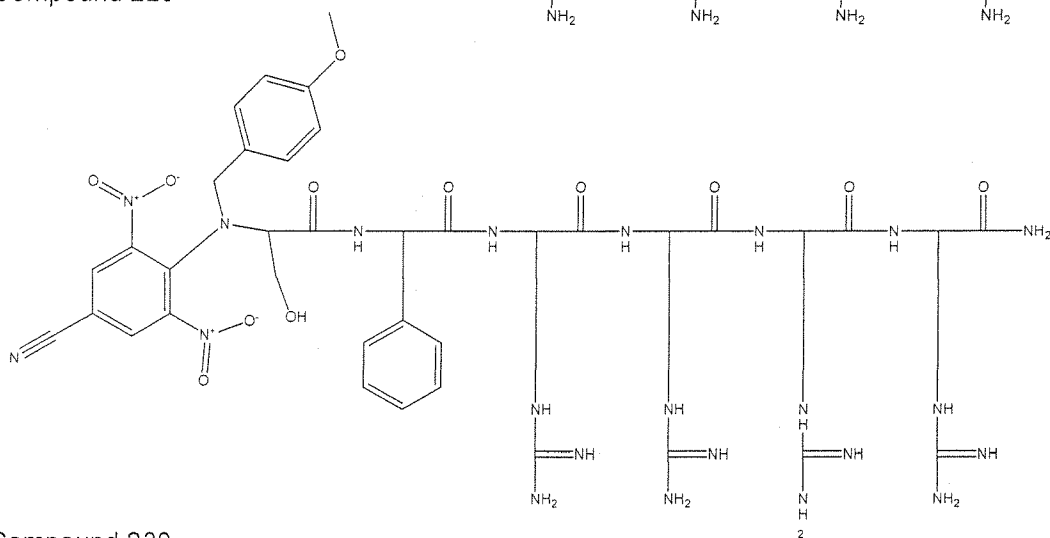


Compound 228

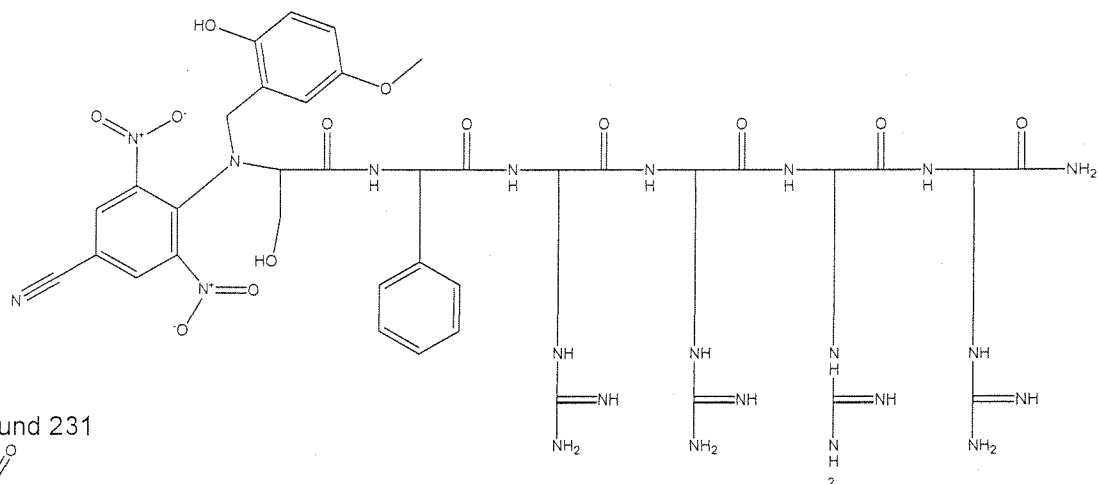
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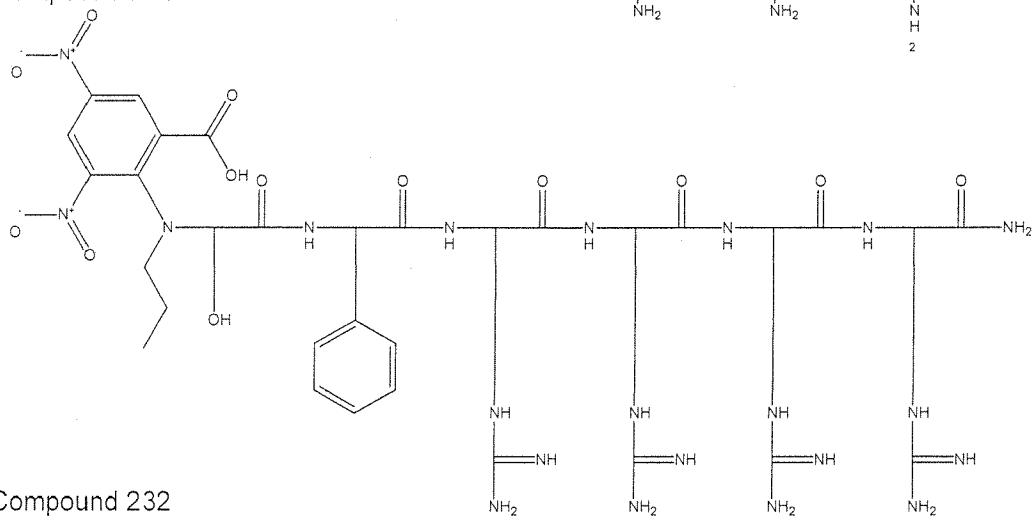
Compound 229



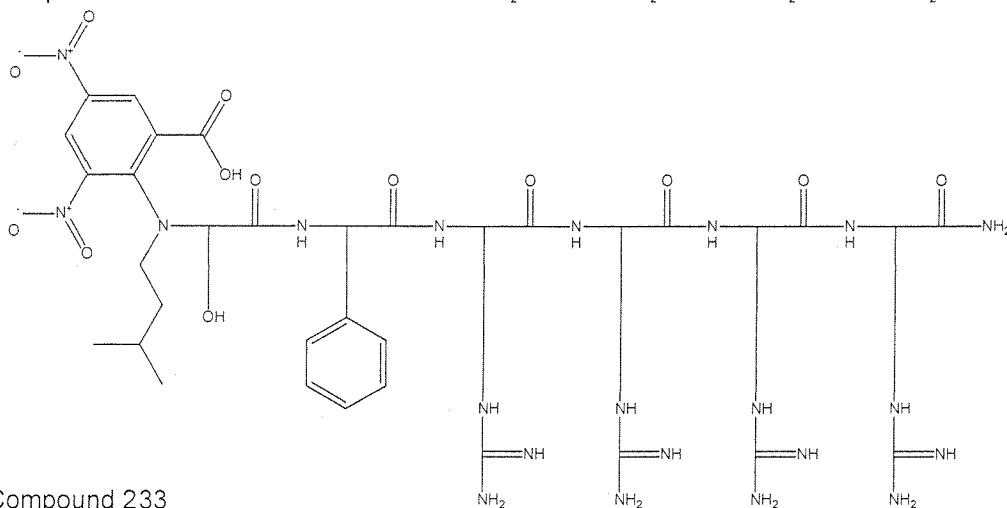
Compound 230



Compound 231

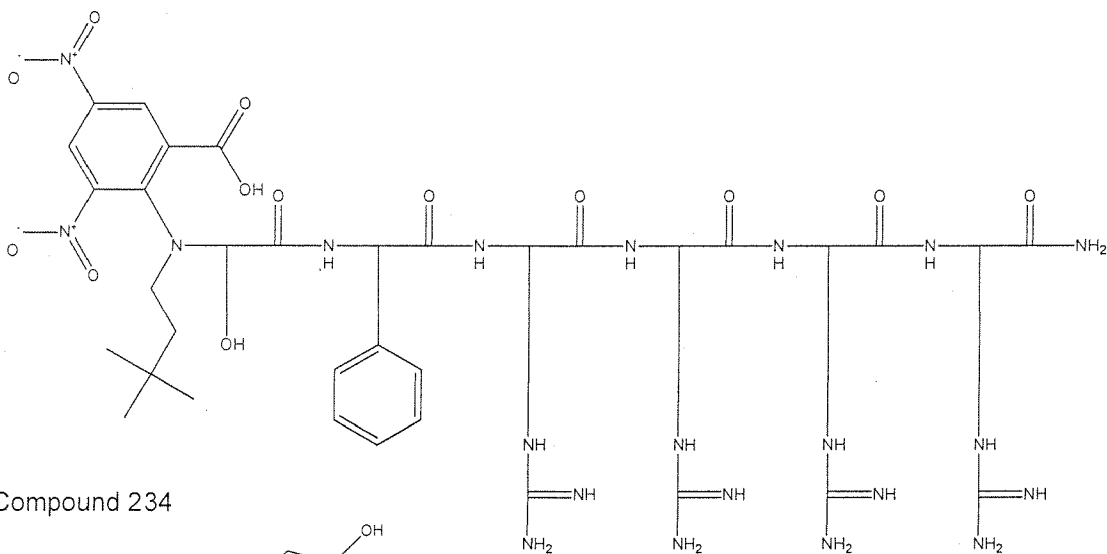


Compound 232

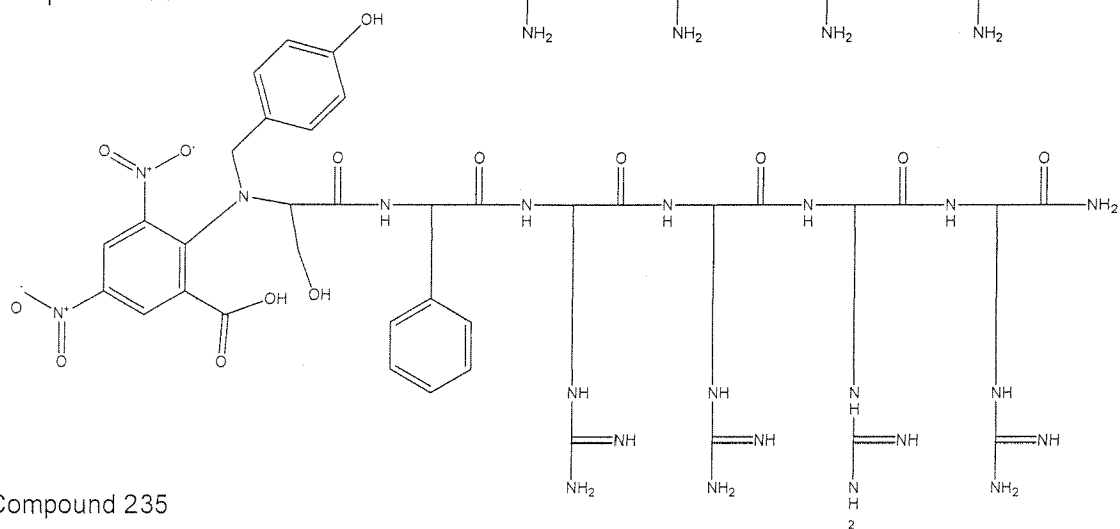


Compound 233

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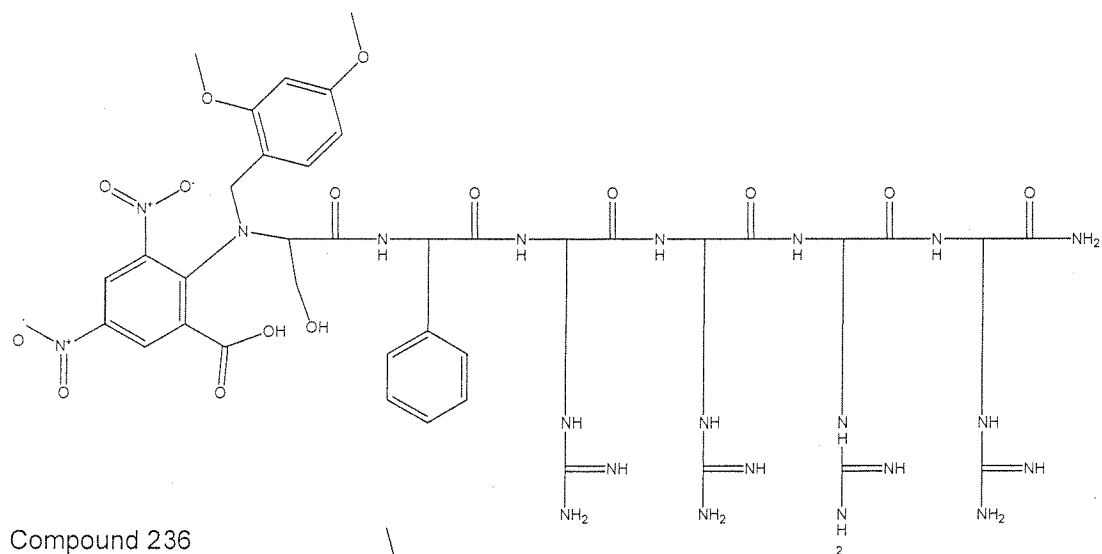


Compound 234

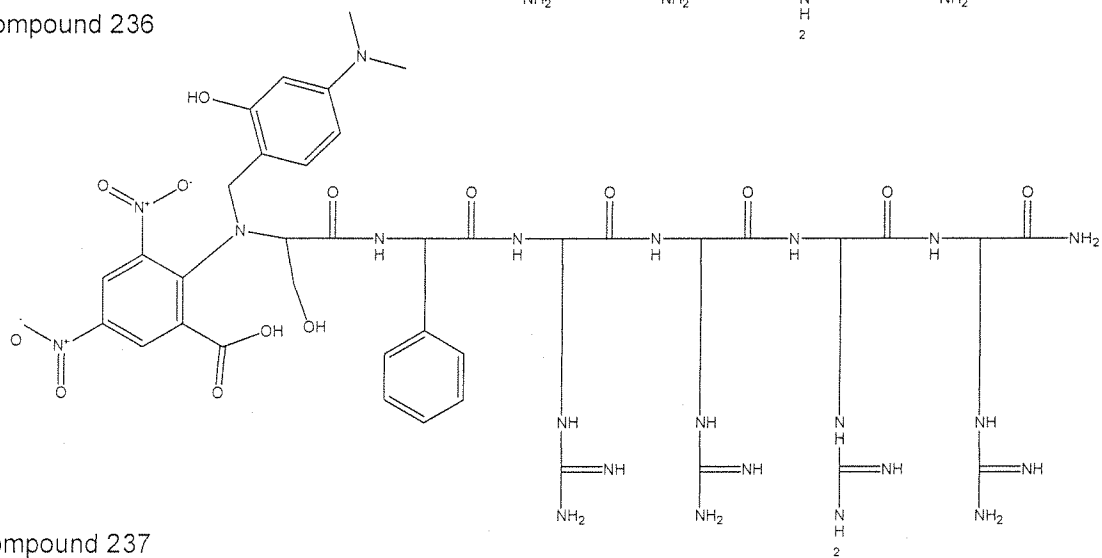


Compound 235

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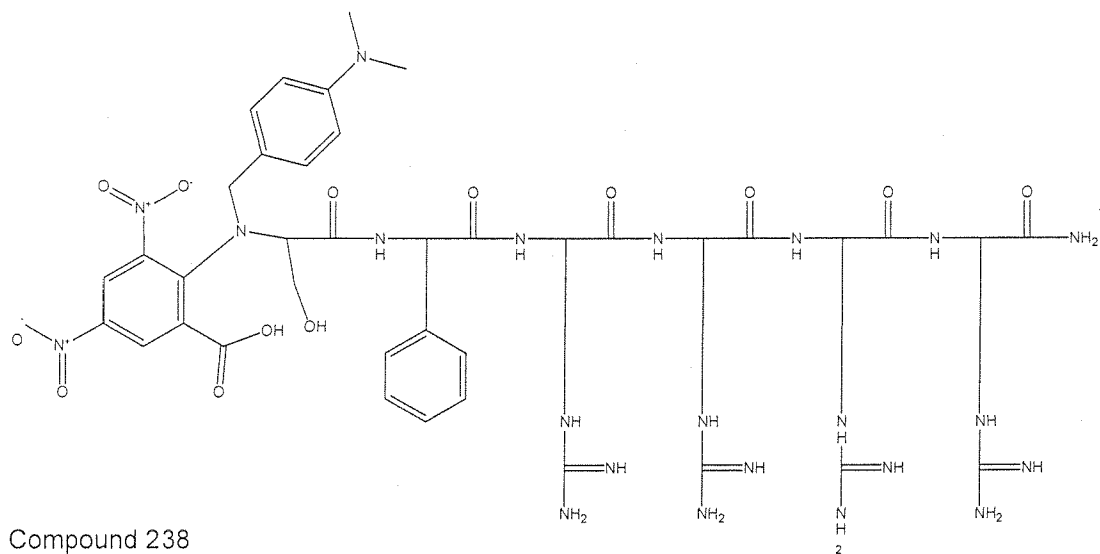


Compound 236

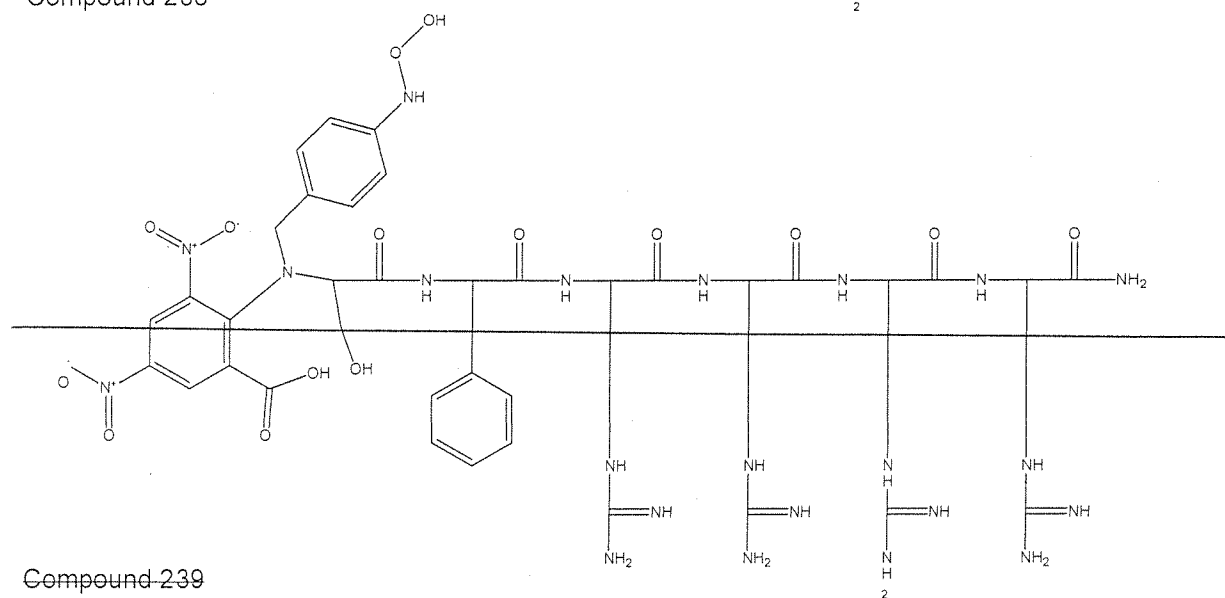


Compound 237

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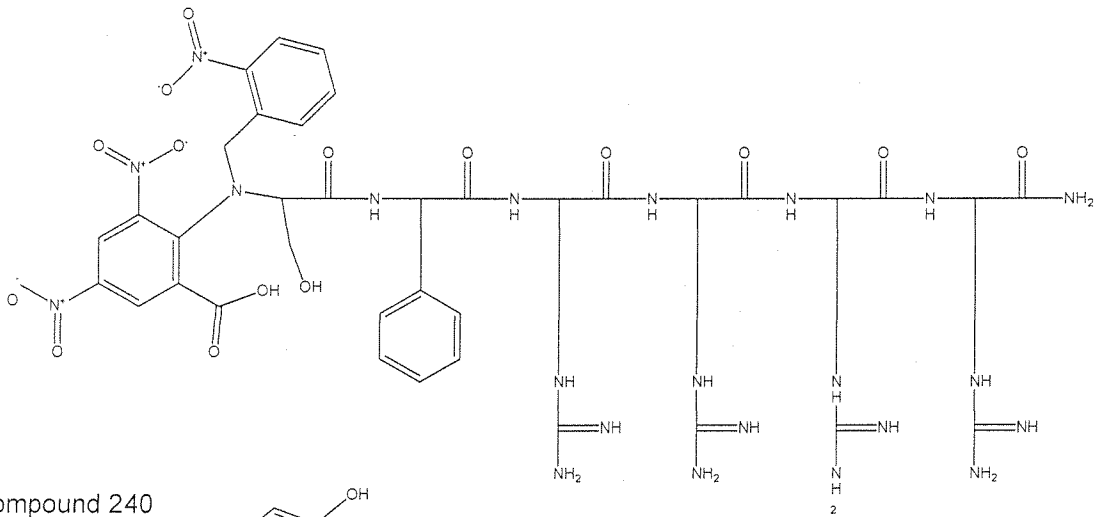


Compound 238

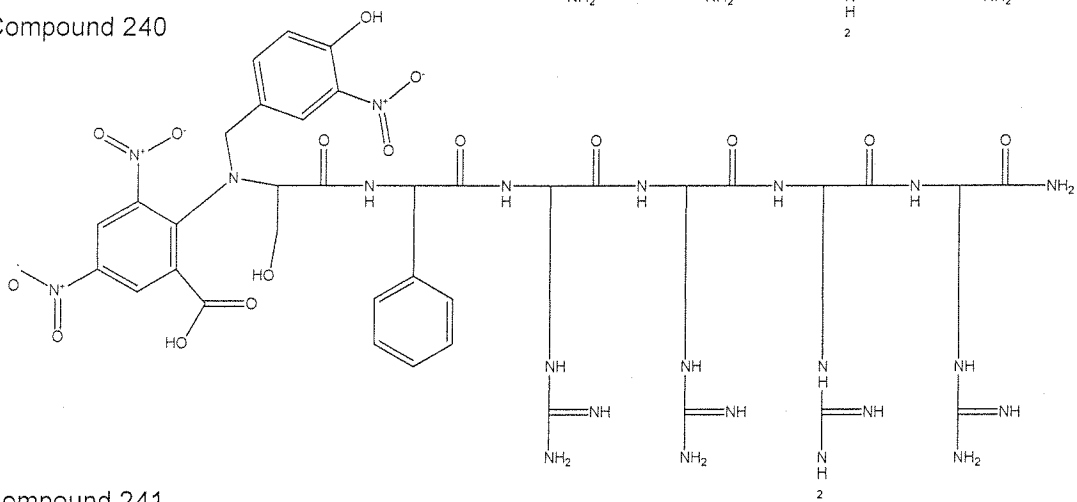


Compound 239

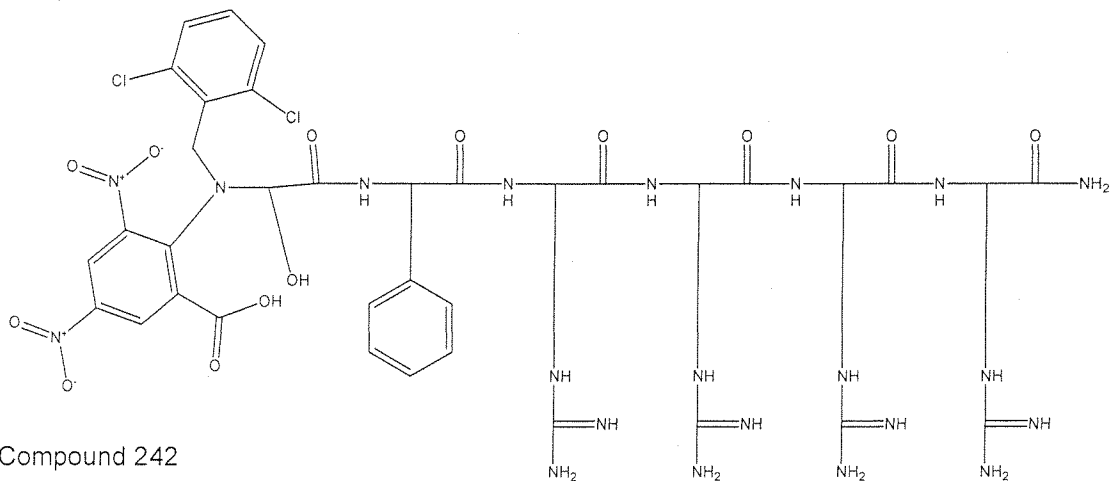
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Compound 240

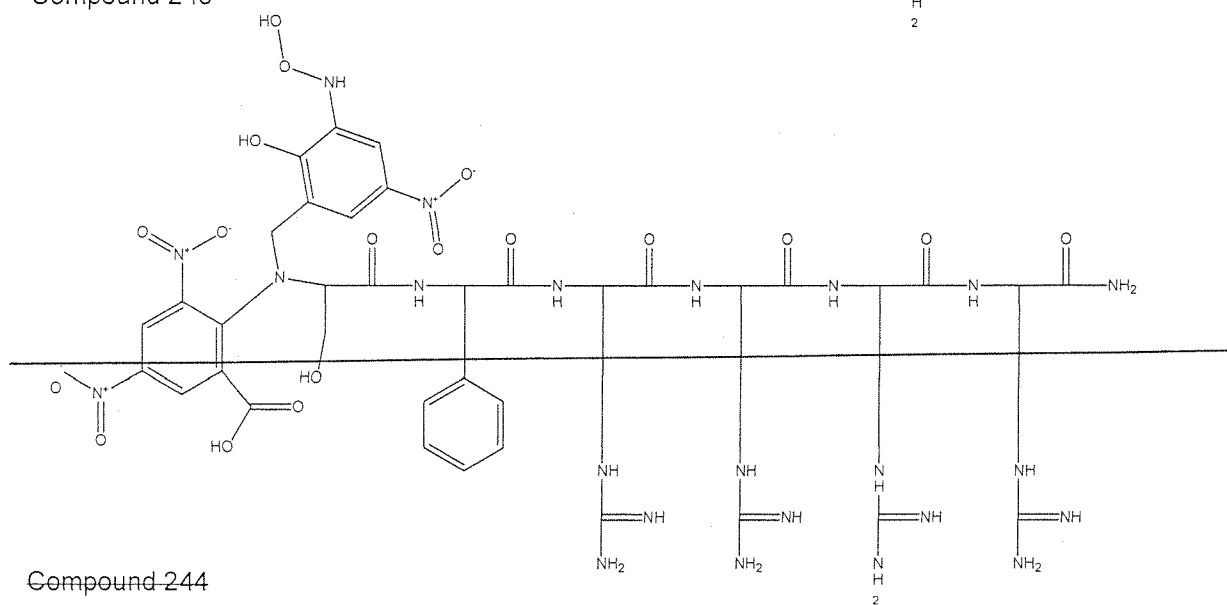
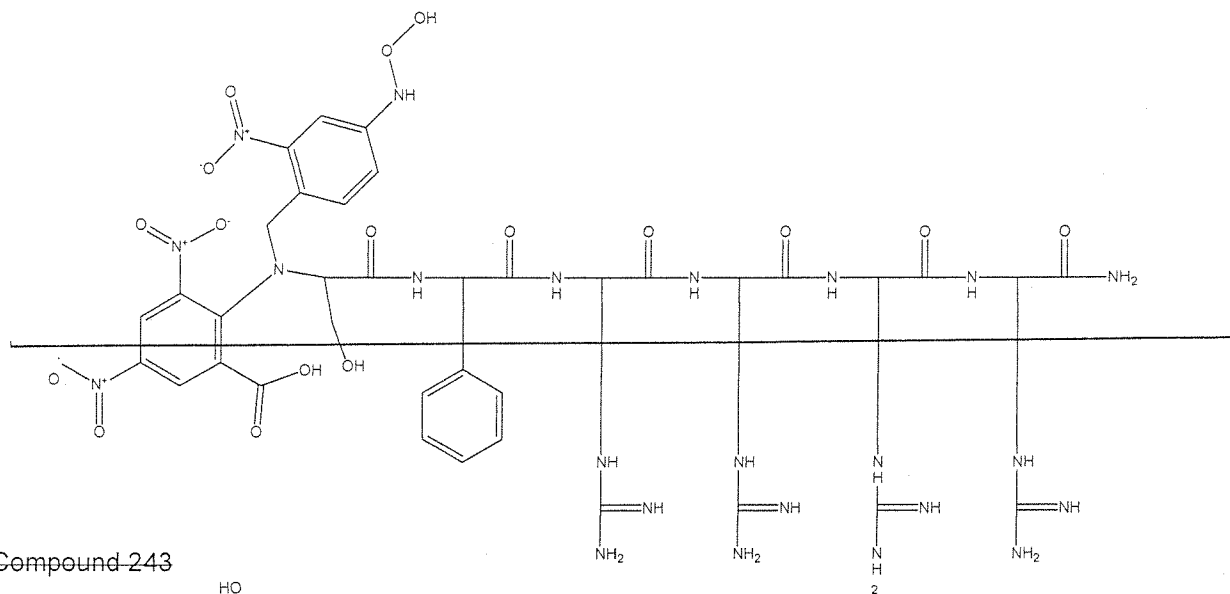


Compound 241

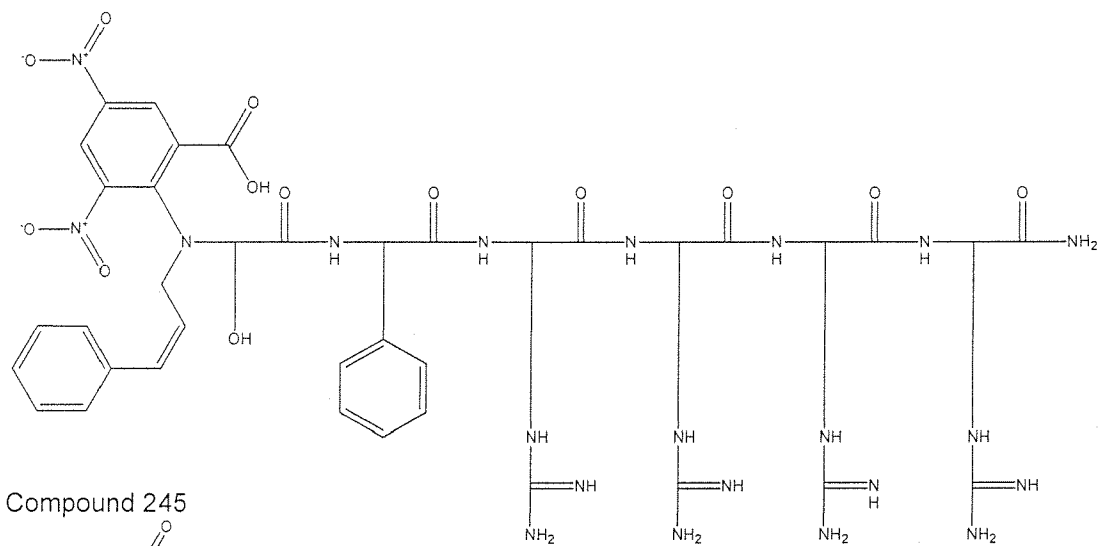


Compound 242

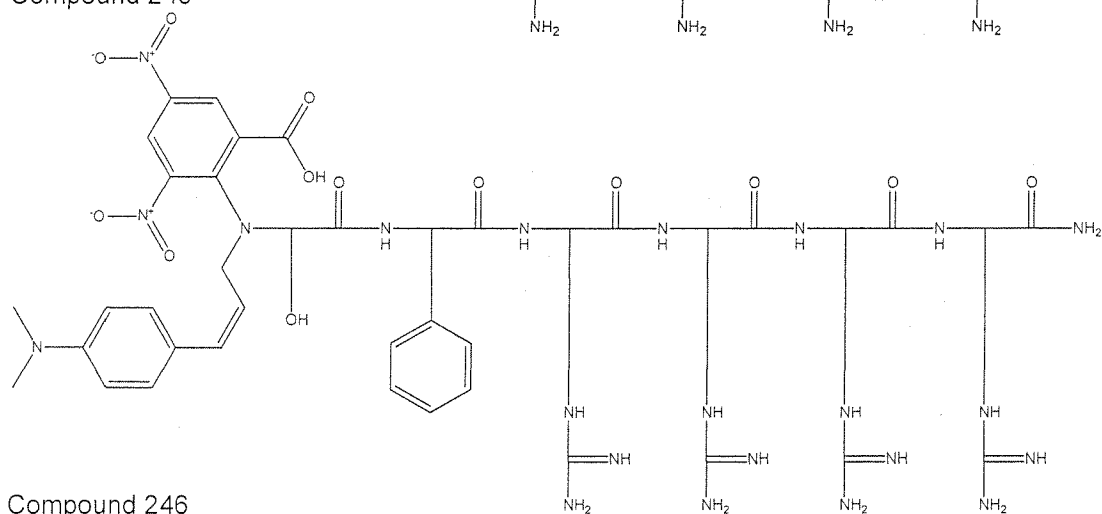
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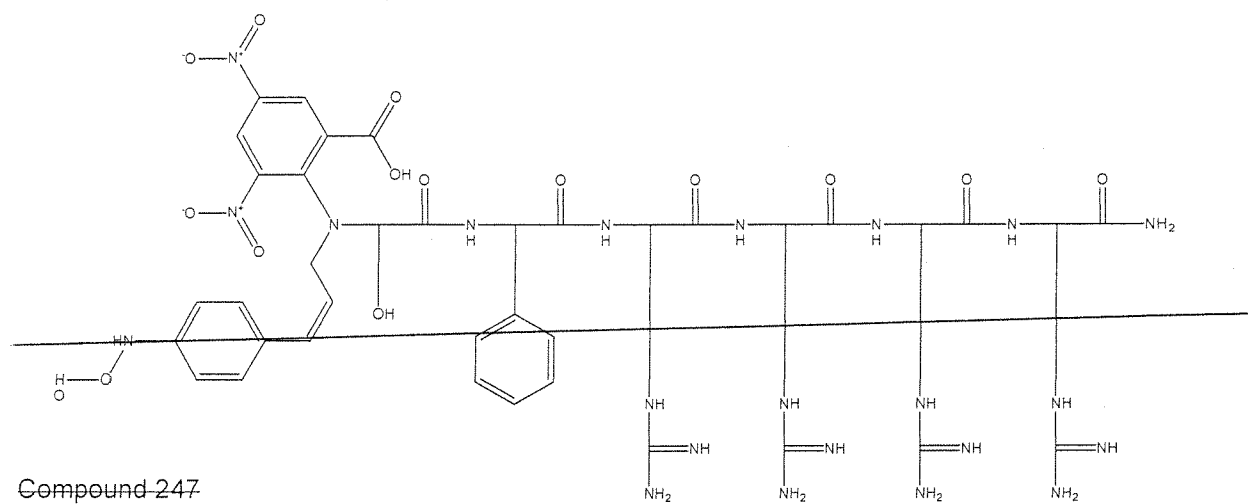


Compound 245

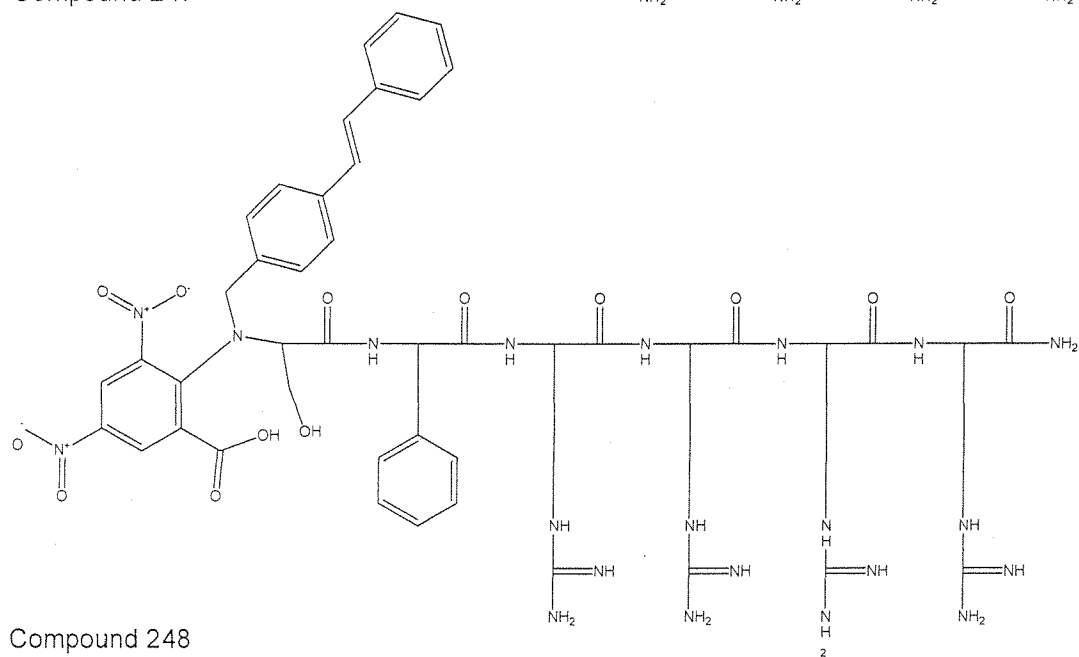


Compound 246

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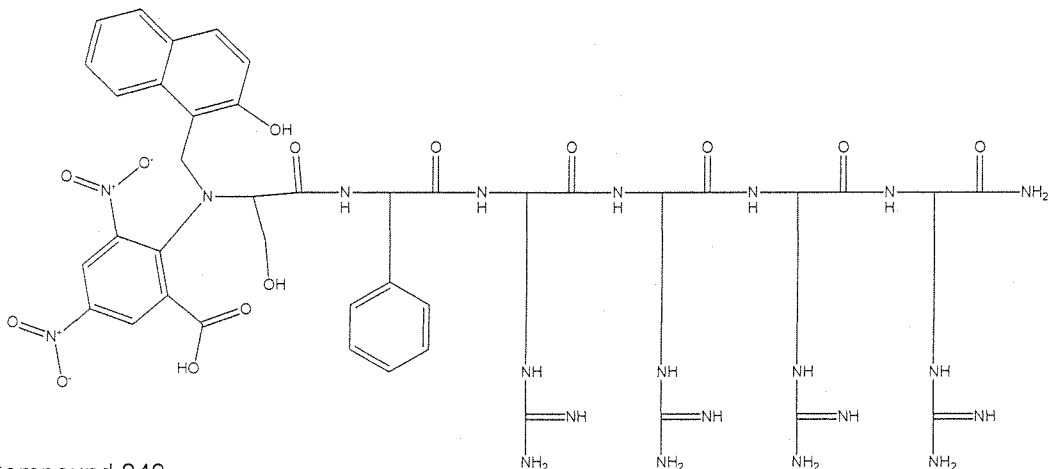


Compound 247

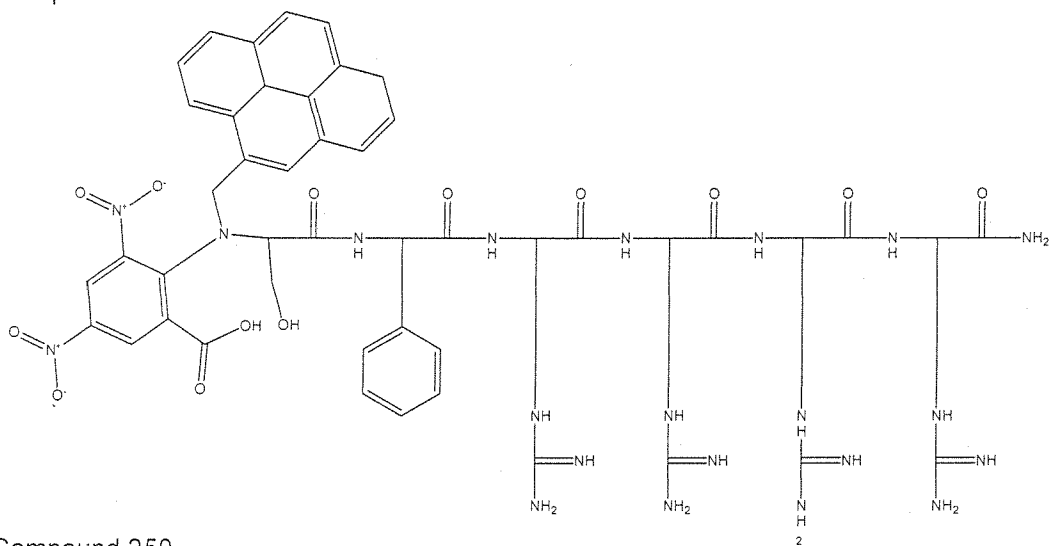


Compound 248

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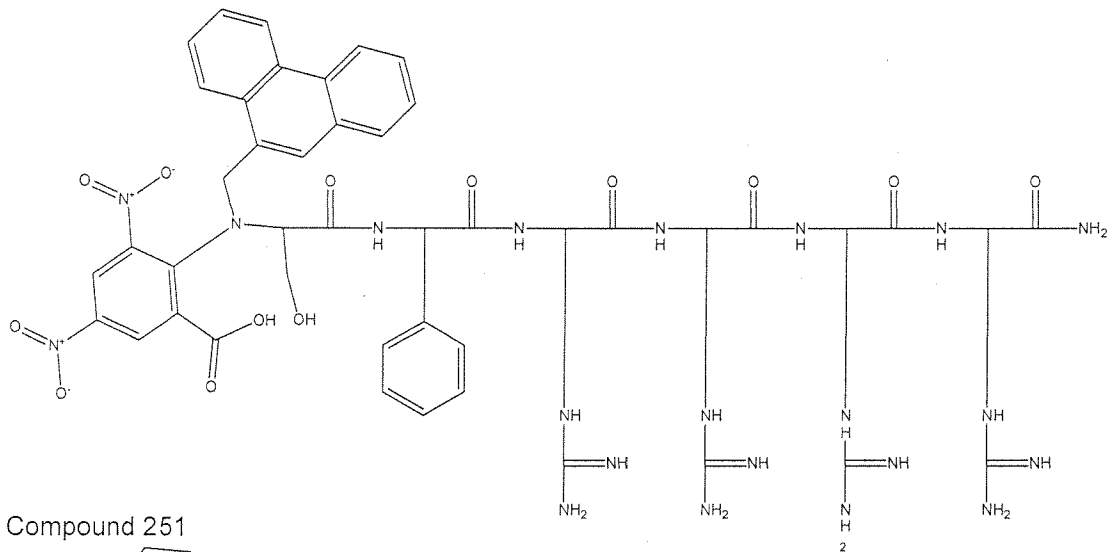


Compound 249

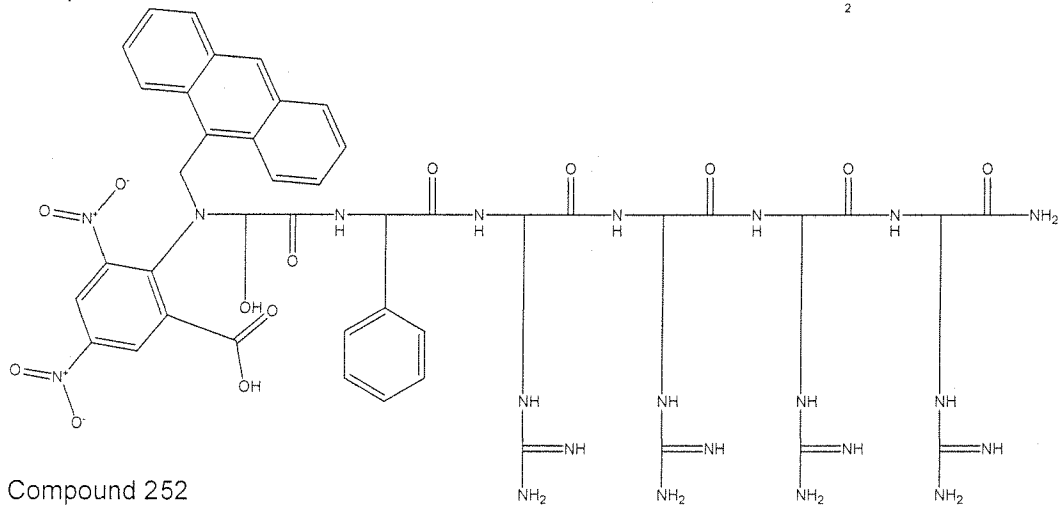


Compound 250

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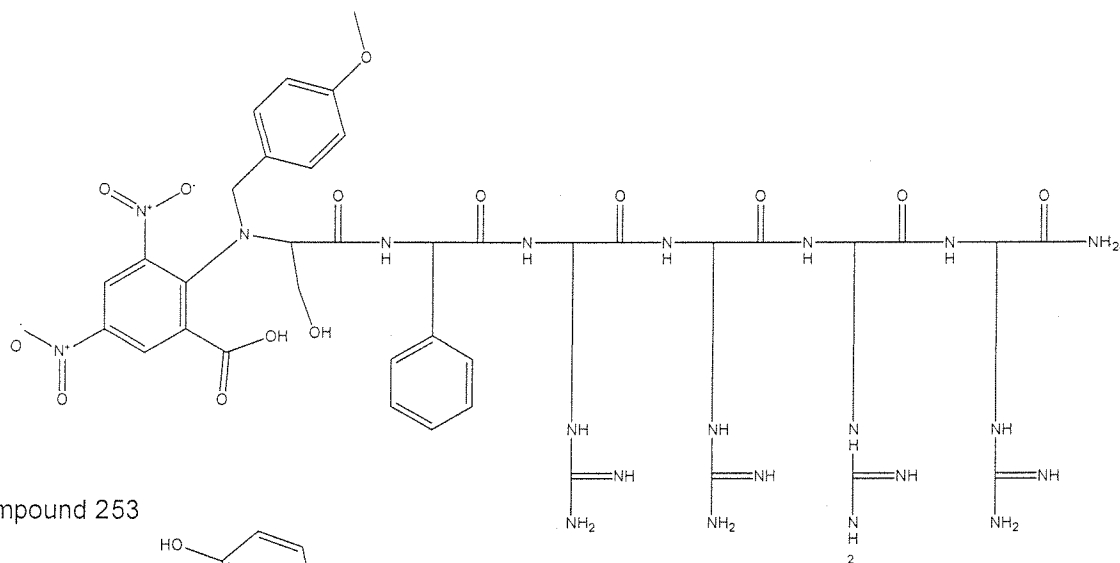


Compound 251

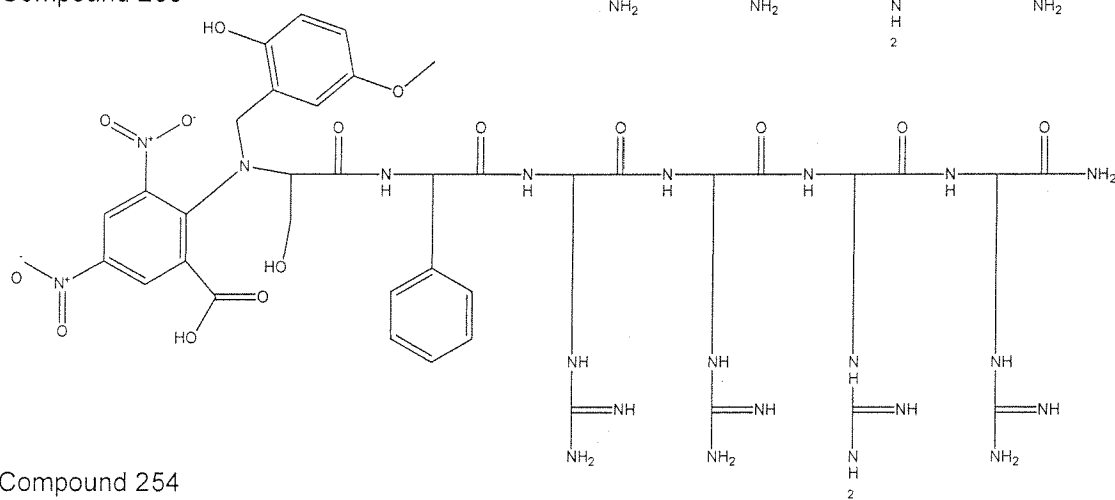


Compound 252

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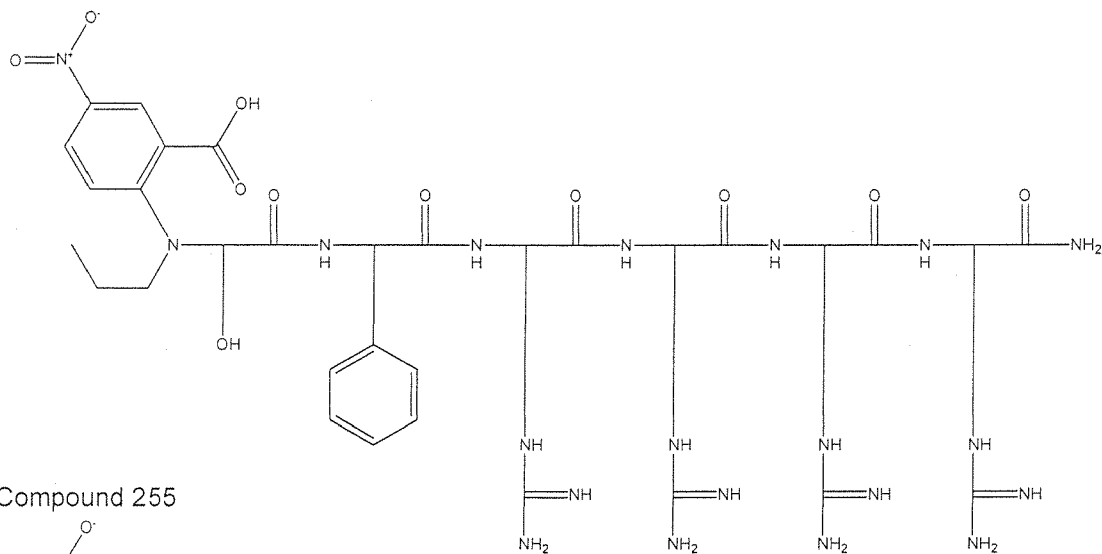


Compound 253

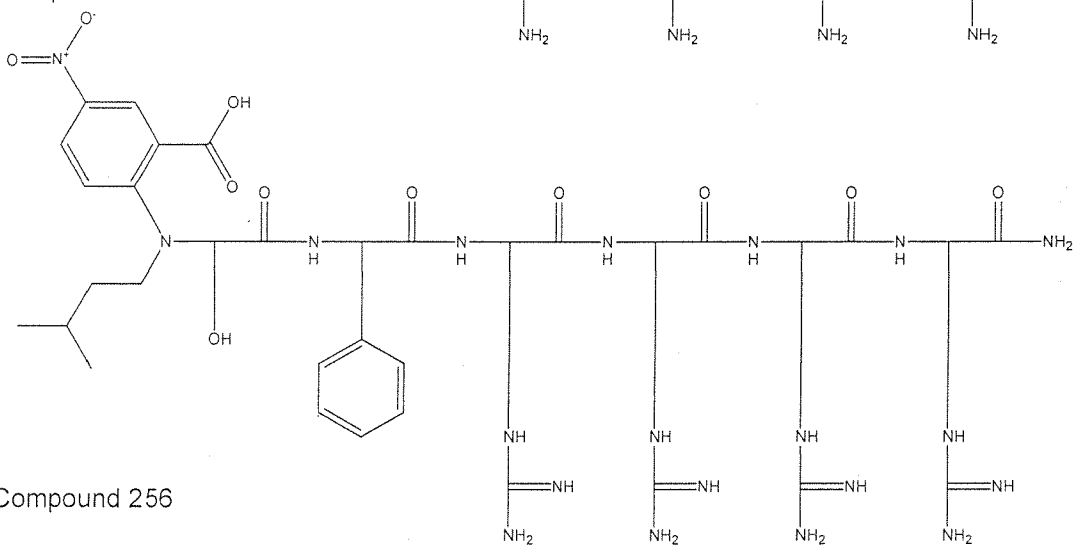


Compound 254

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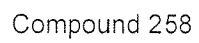


Compound 255

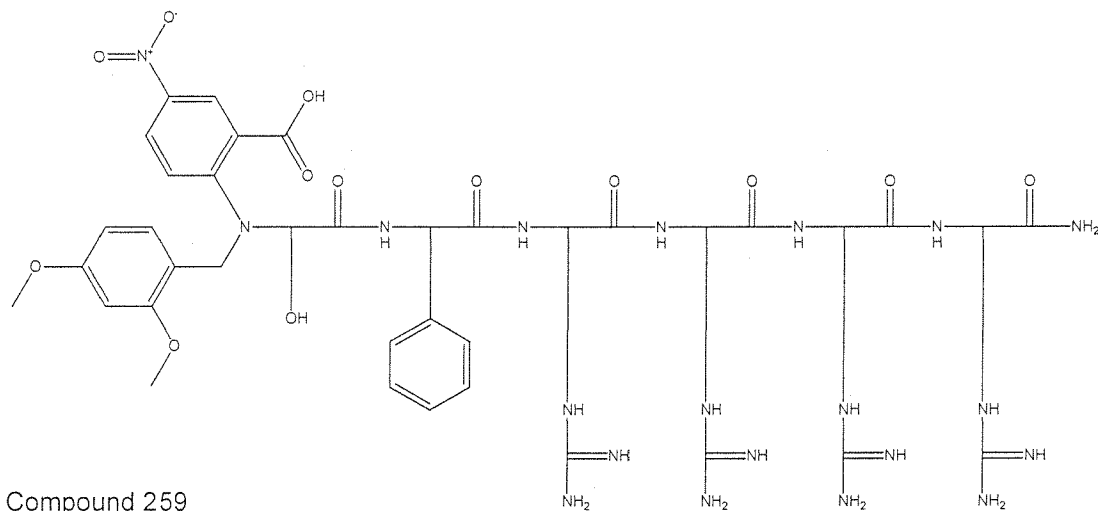


Compound 256

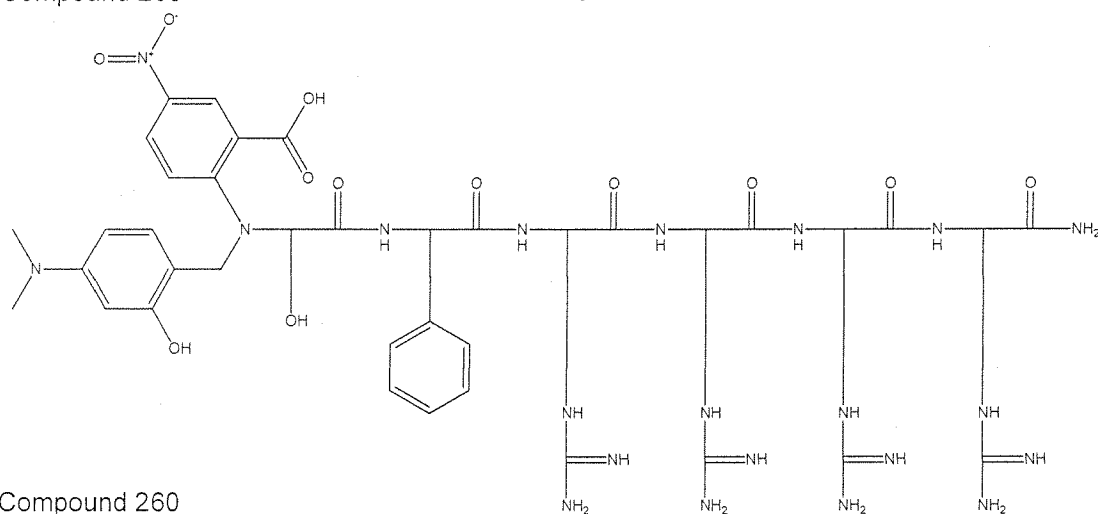
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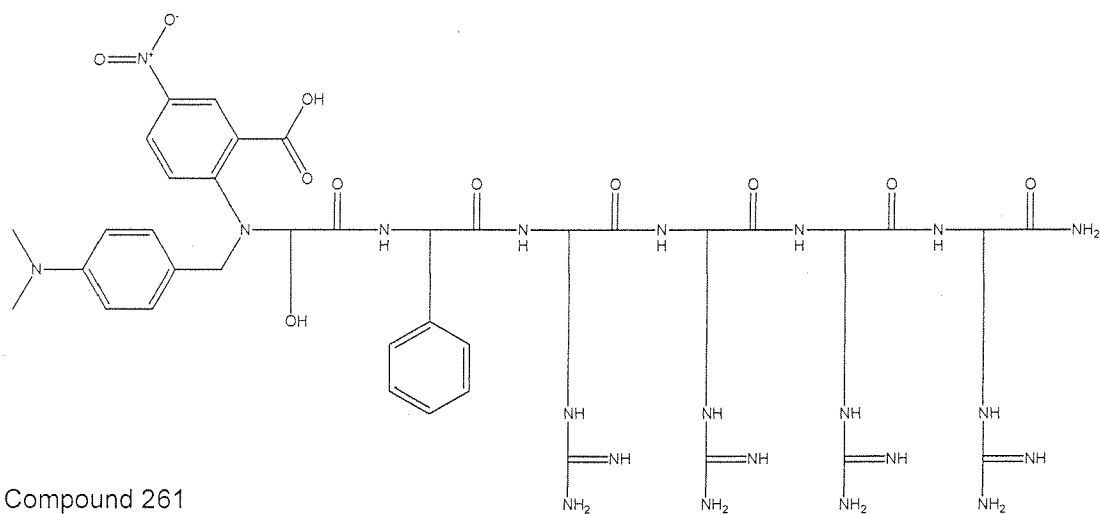


Compound 259

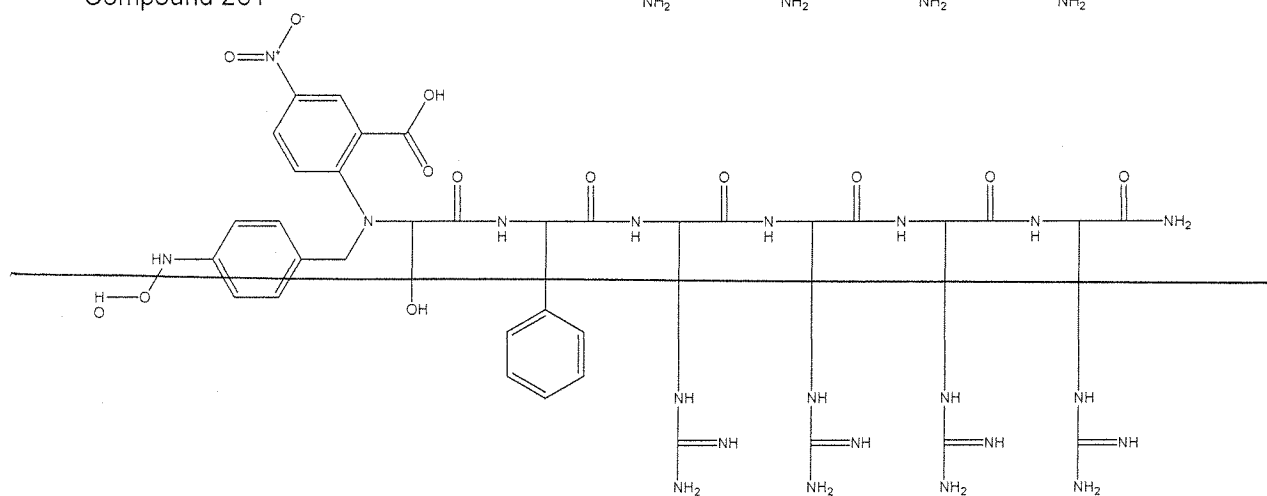


Compound 260

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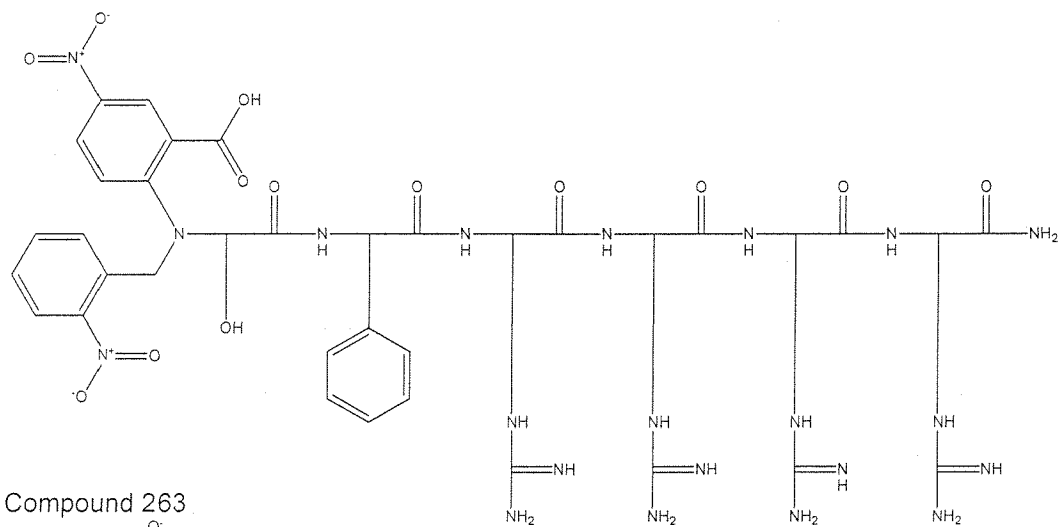


Compound 261

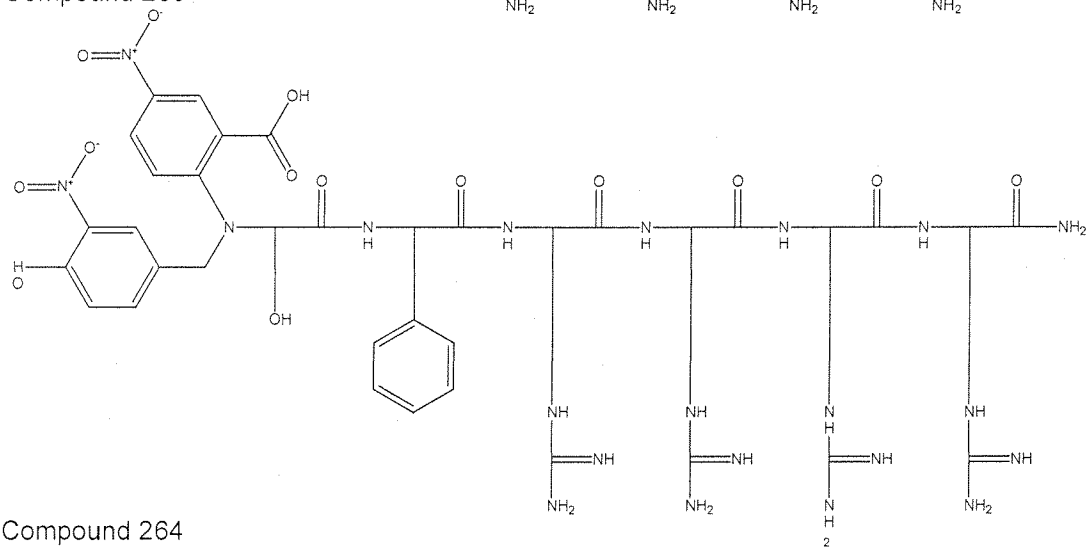


Compound 262

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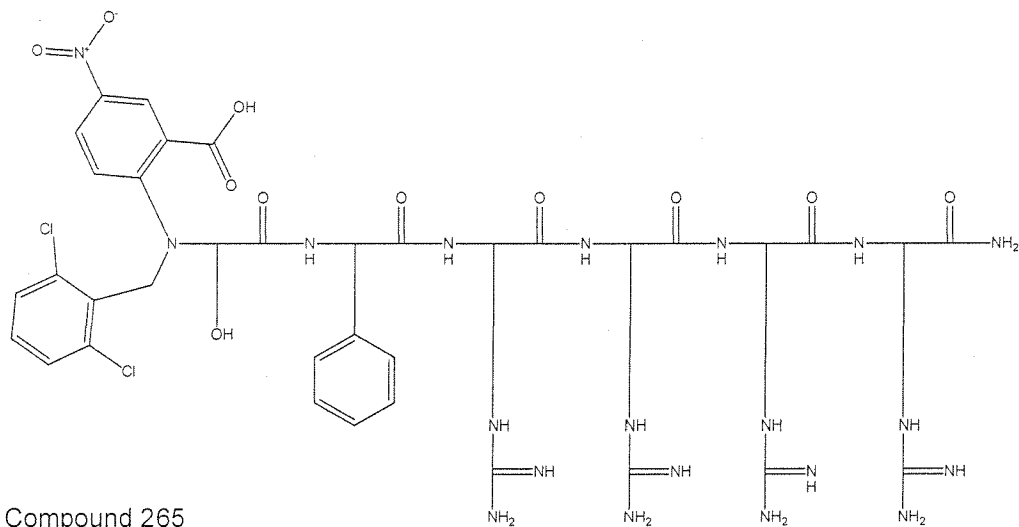


Compound 263

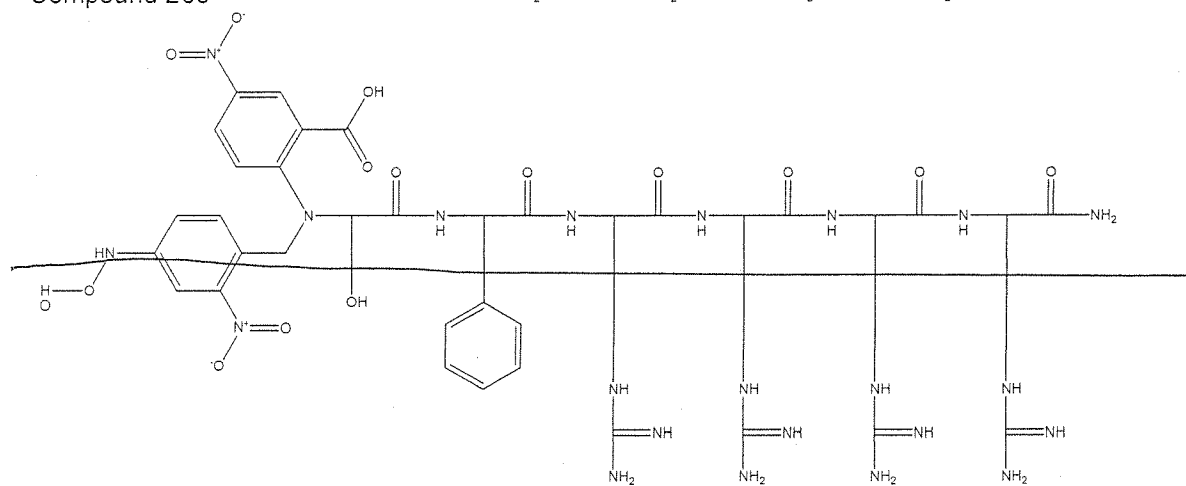


Compound 264

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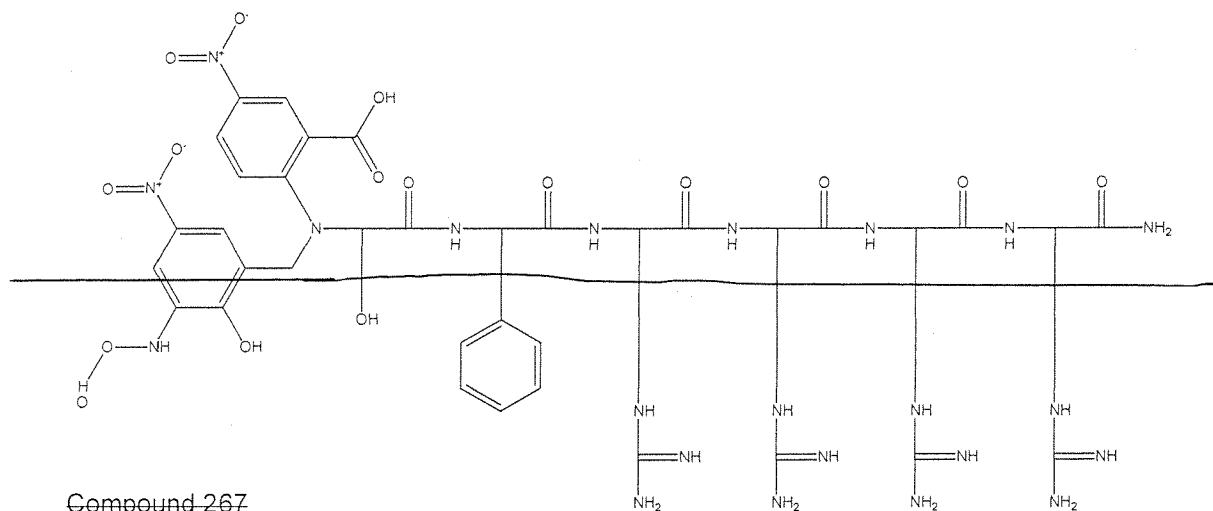


Compound 265

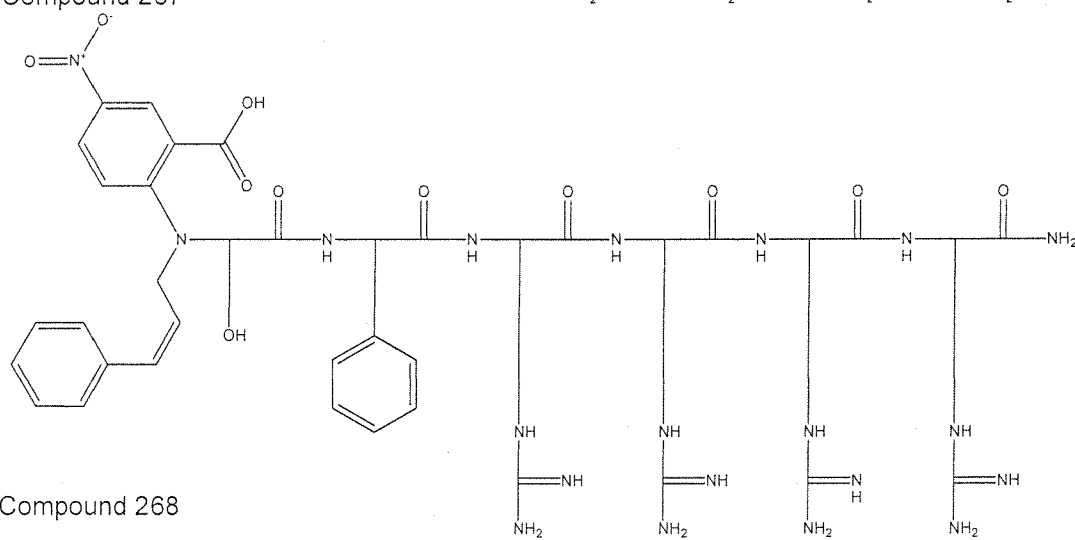


Compound 266

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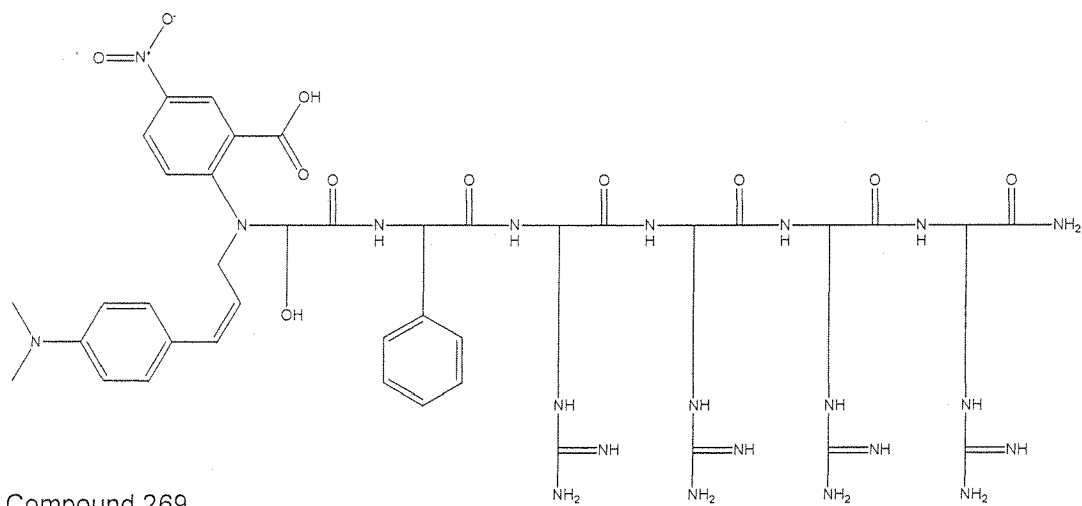


Compound 267

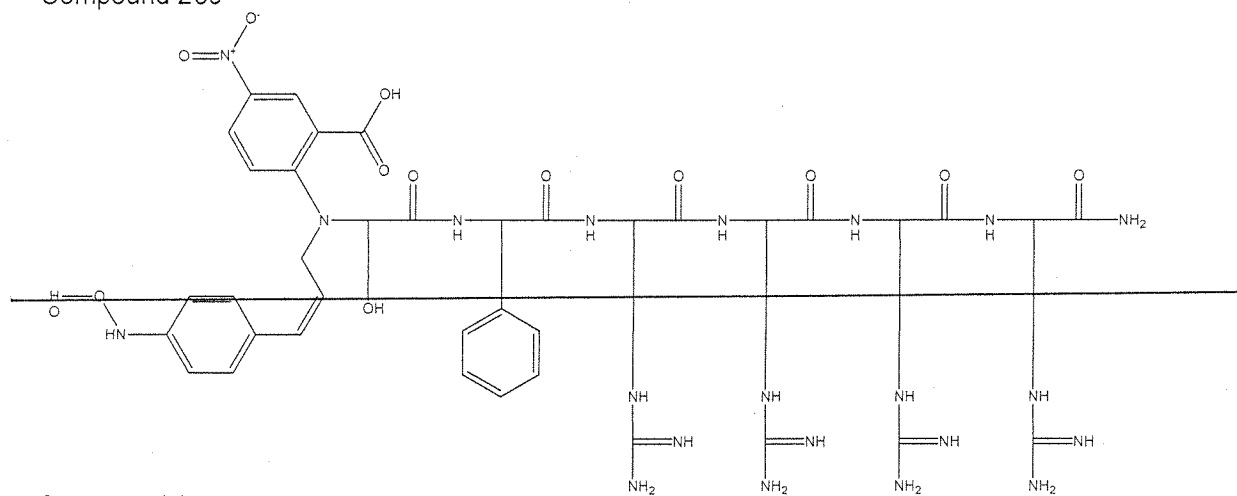


Compound 268

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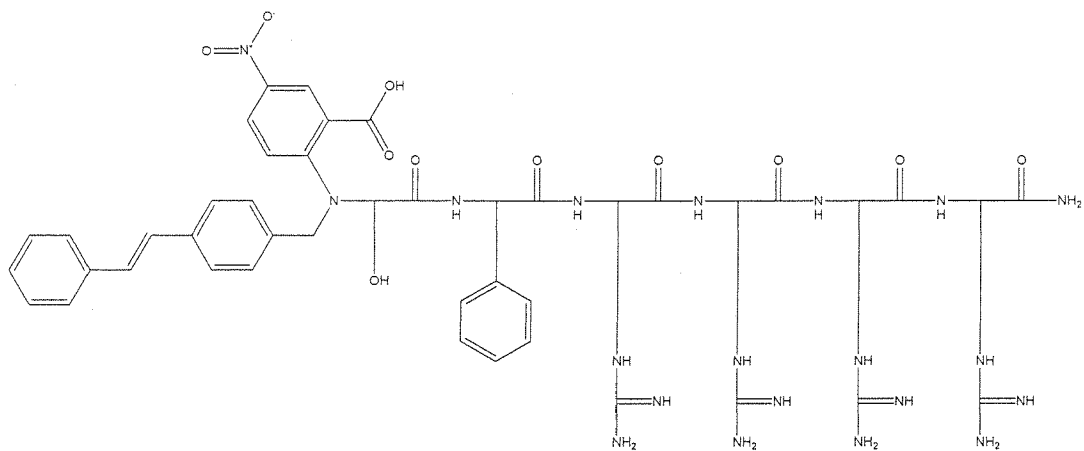


Compound 269

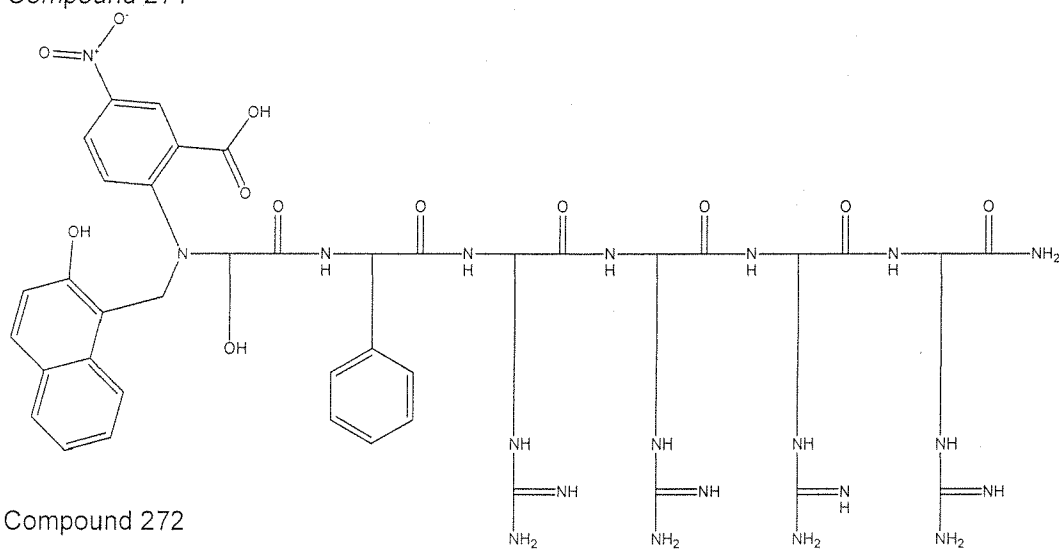


Compound 270

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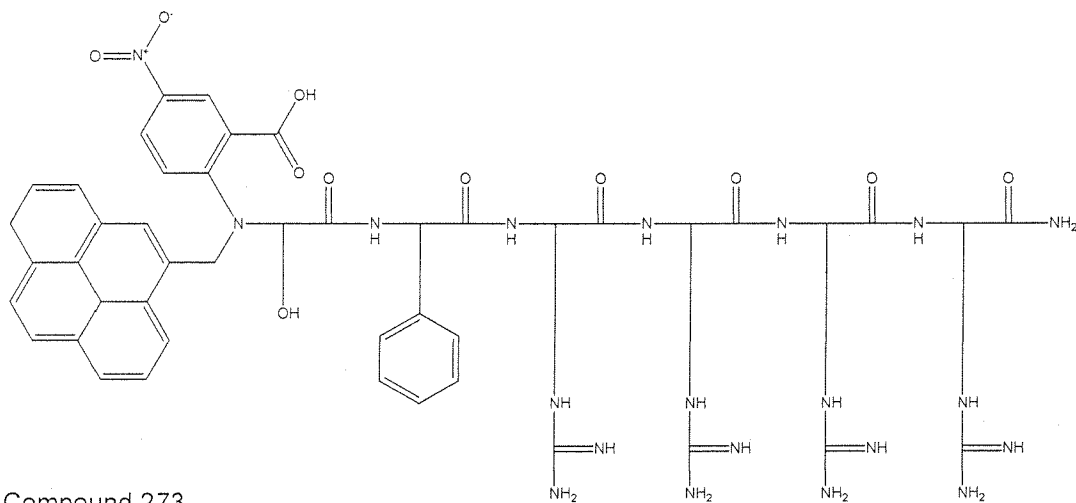


Compound 271

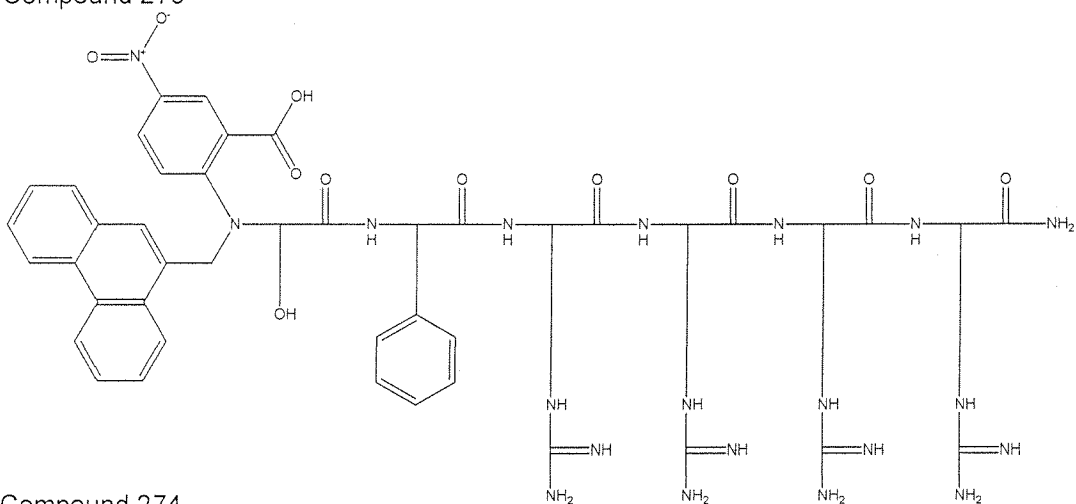


Compound 272

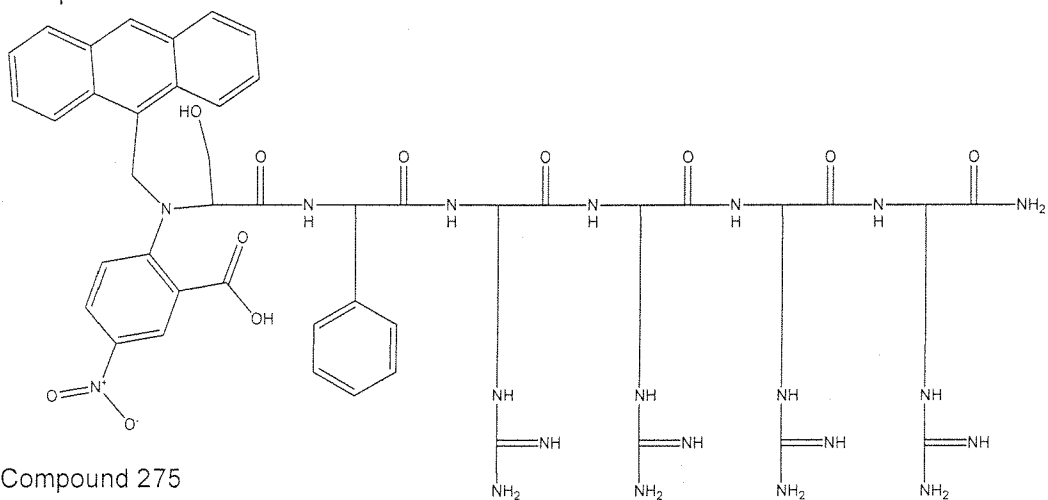
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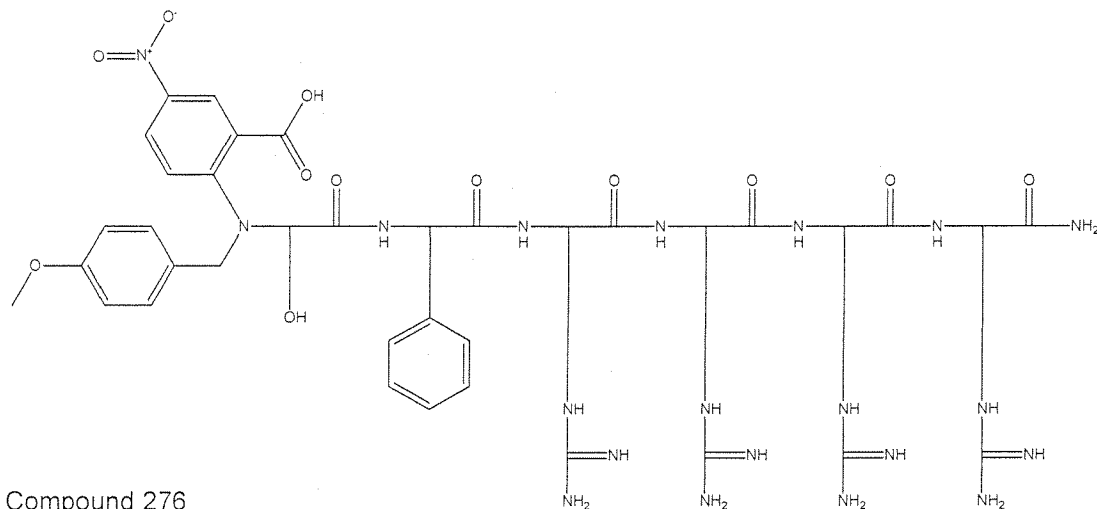
Compound 273



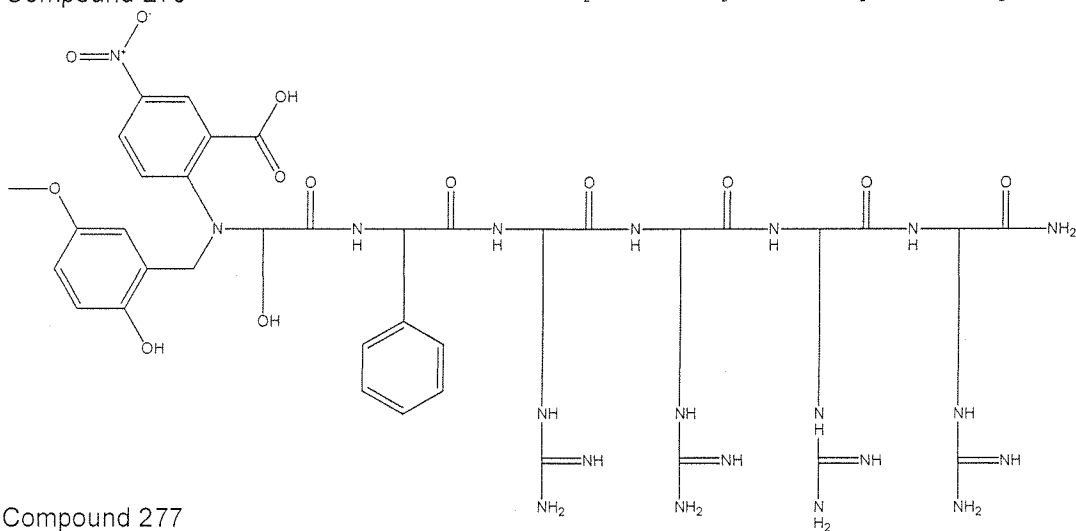
Compound 274



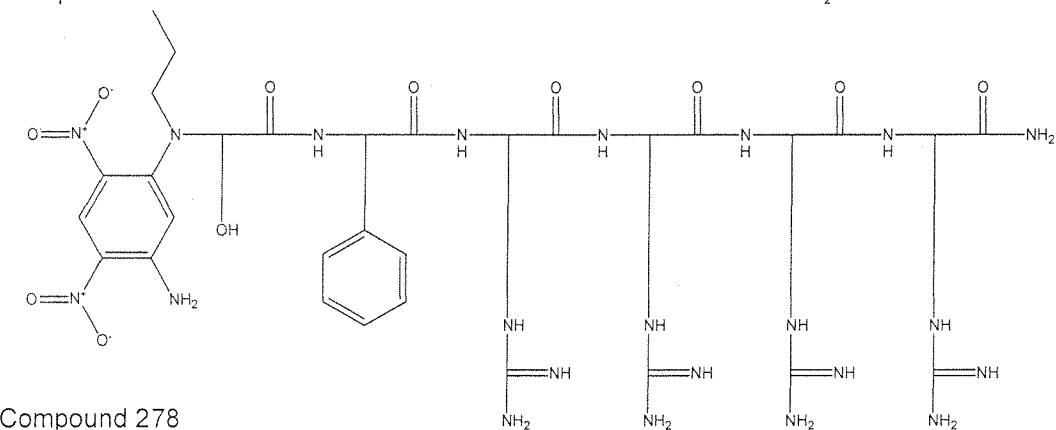
Compound 275



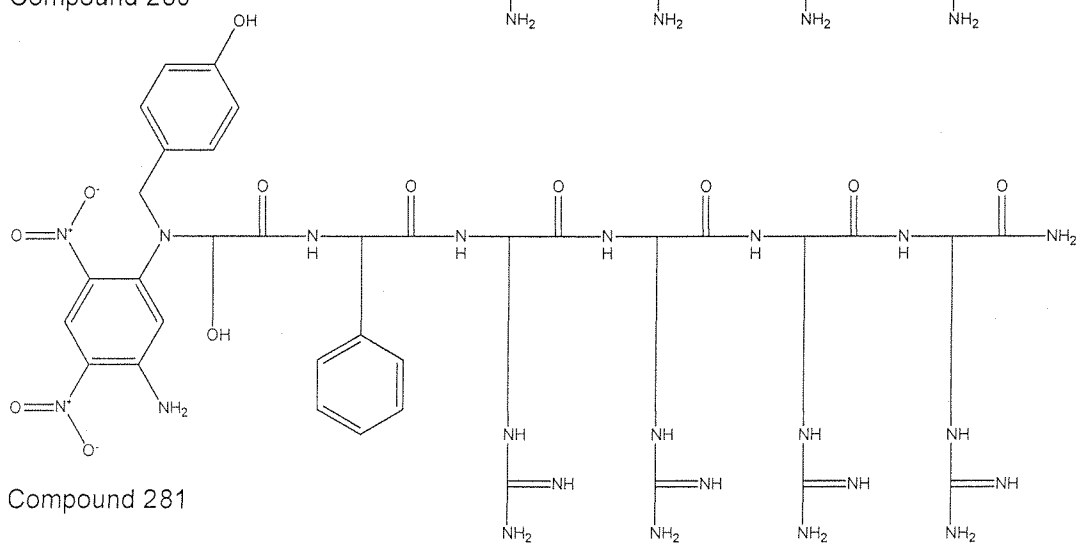
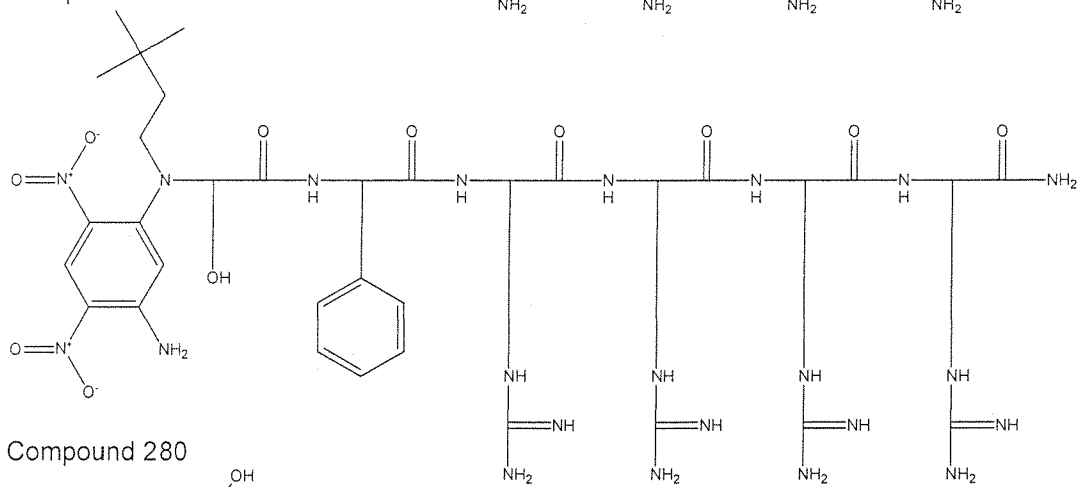
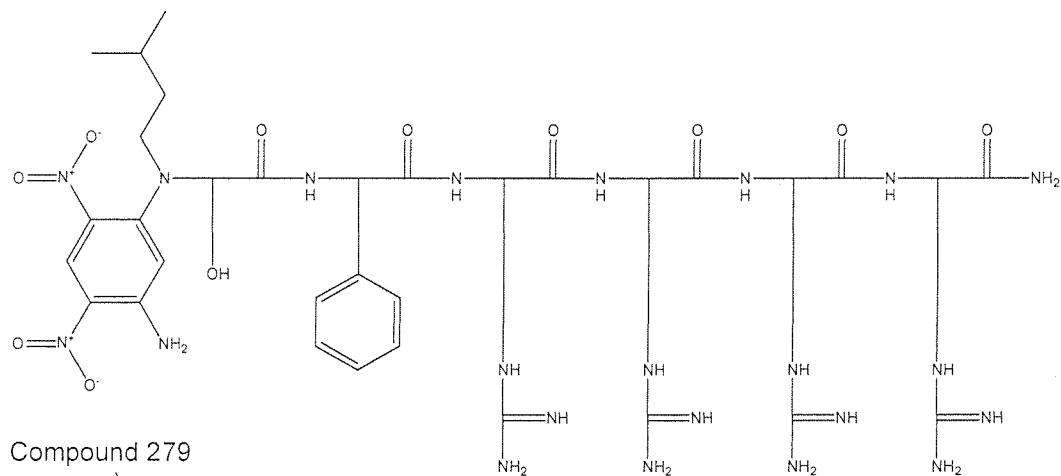
Compound 276



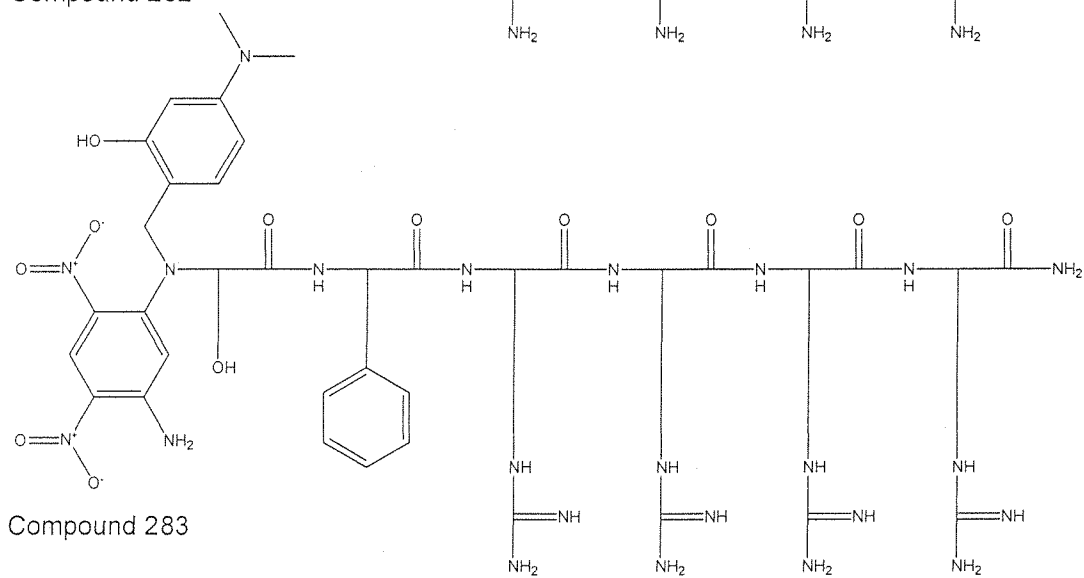
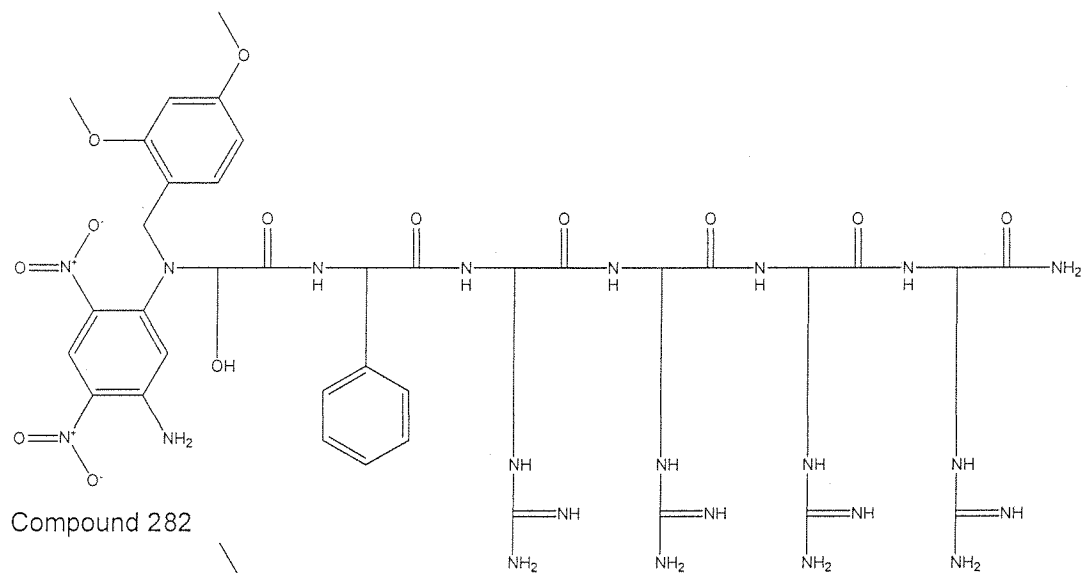
Compound 277



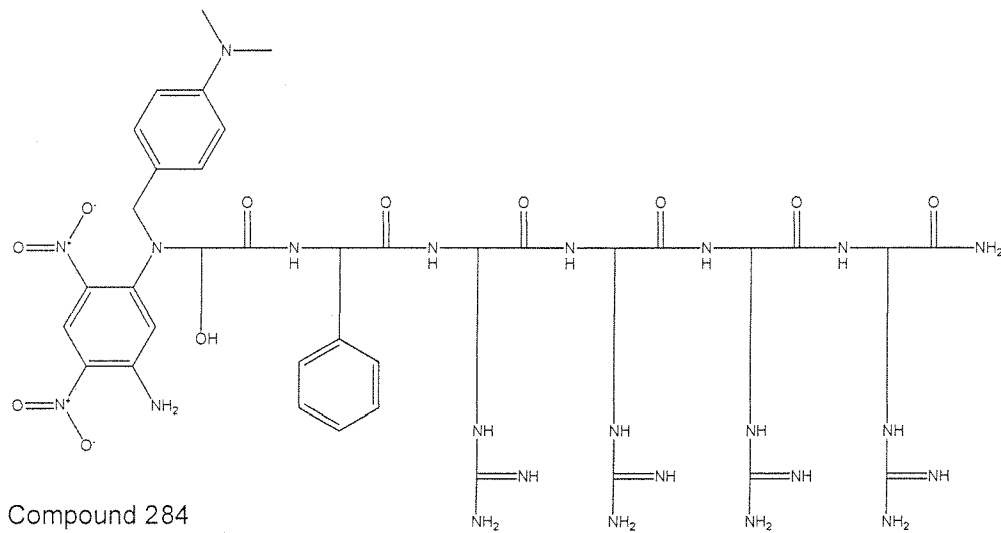
Compound 278



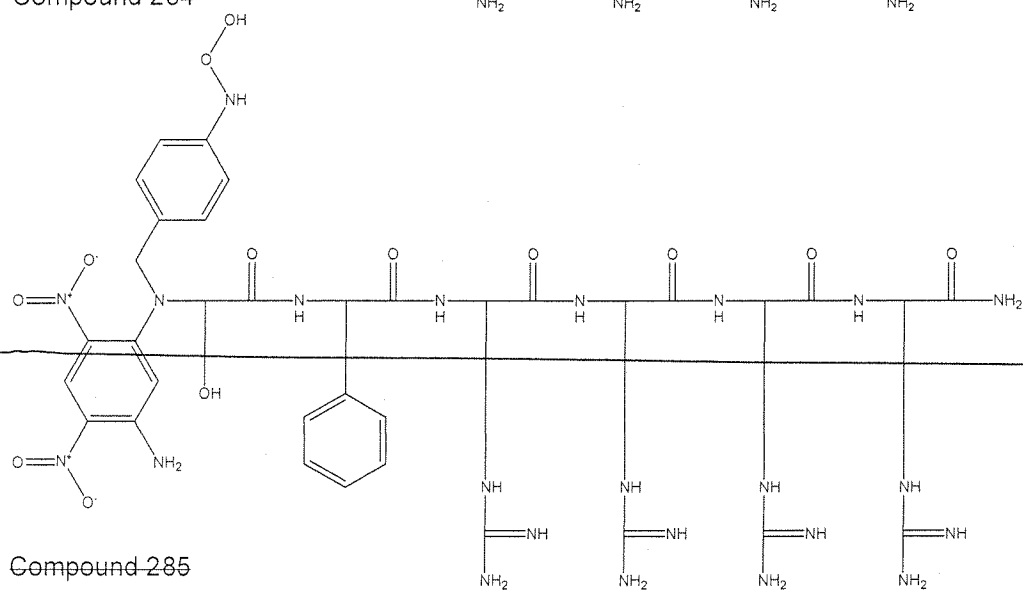
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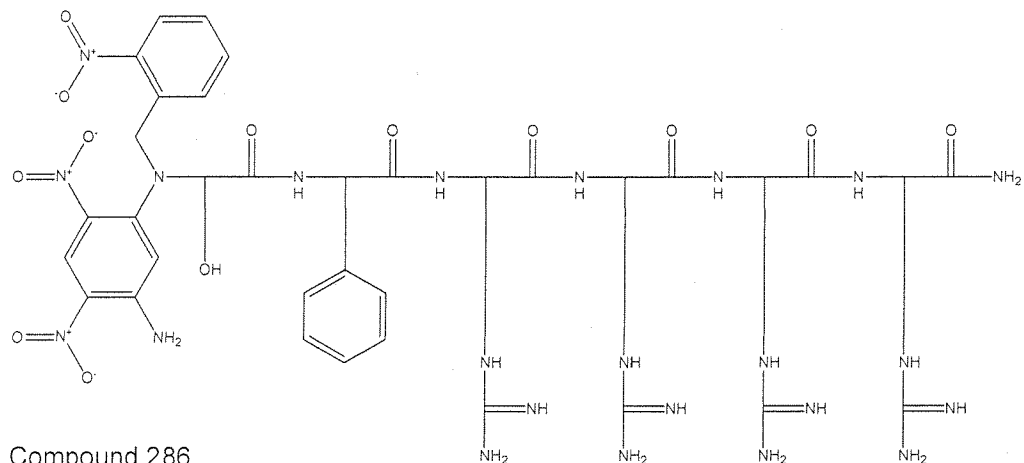
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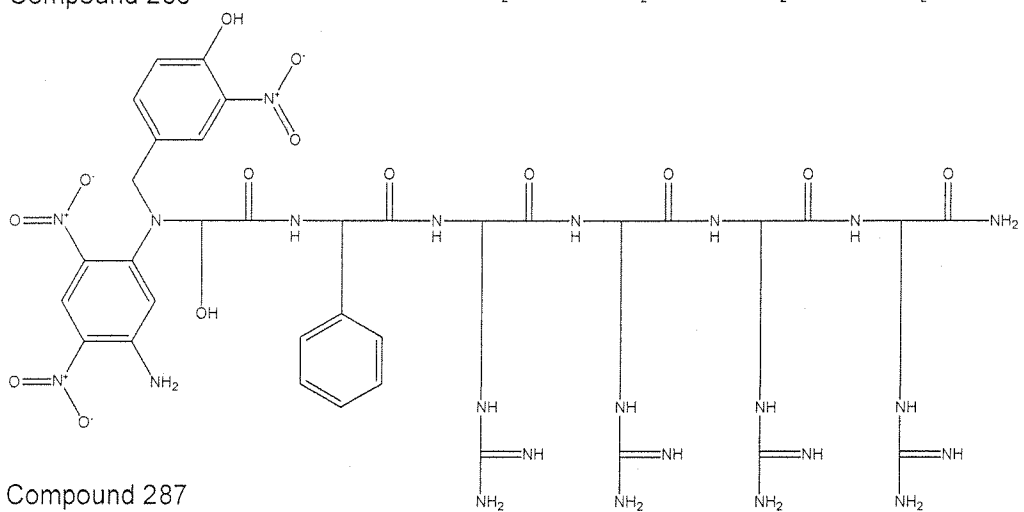
Compound 284



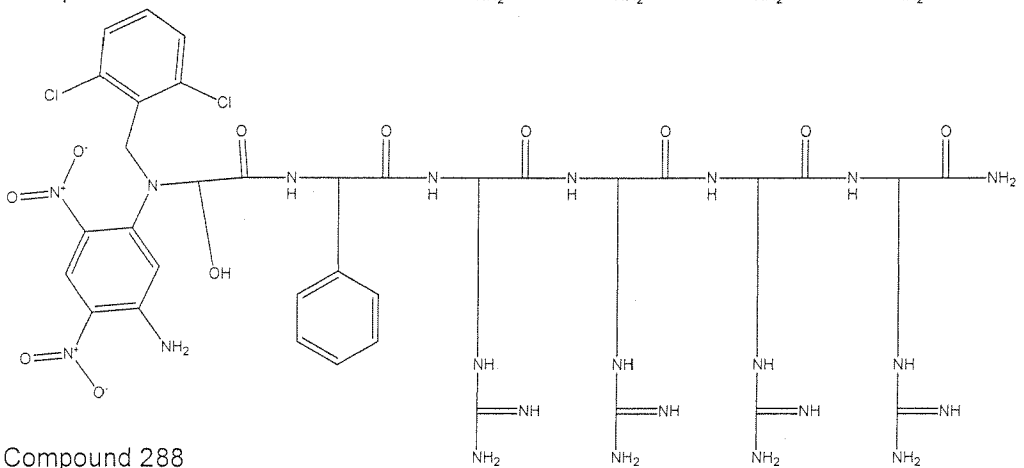
Compound 285



Compound 286

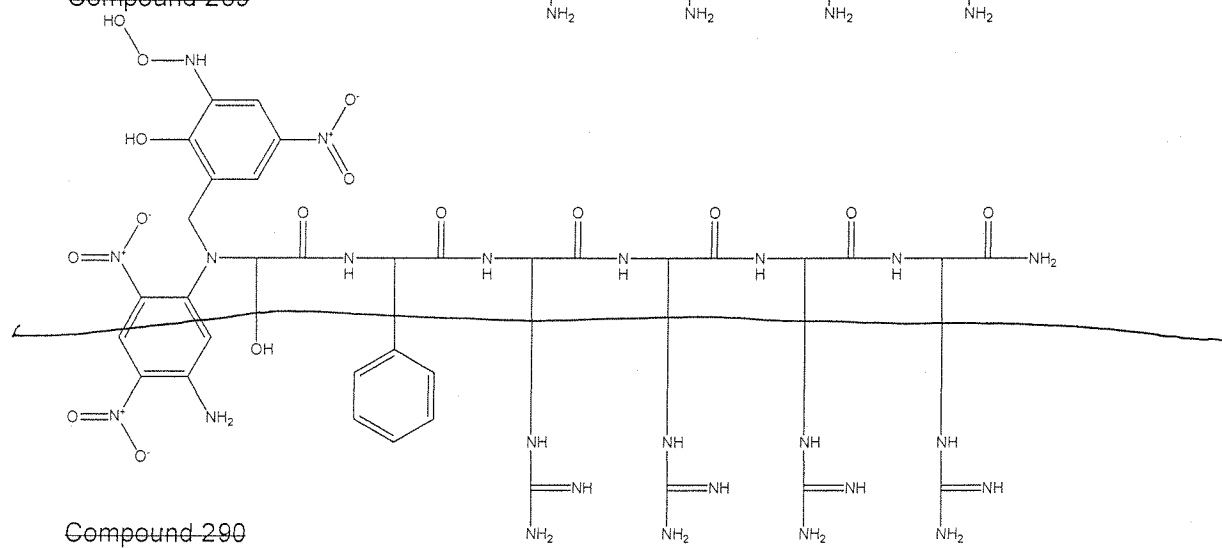
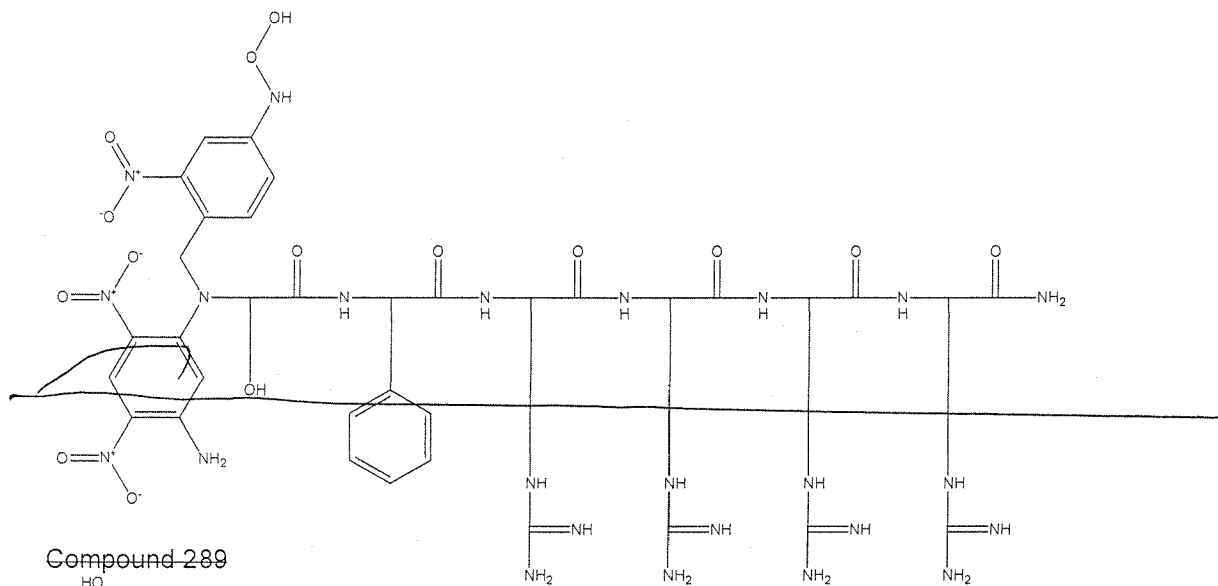


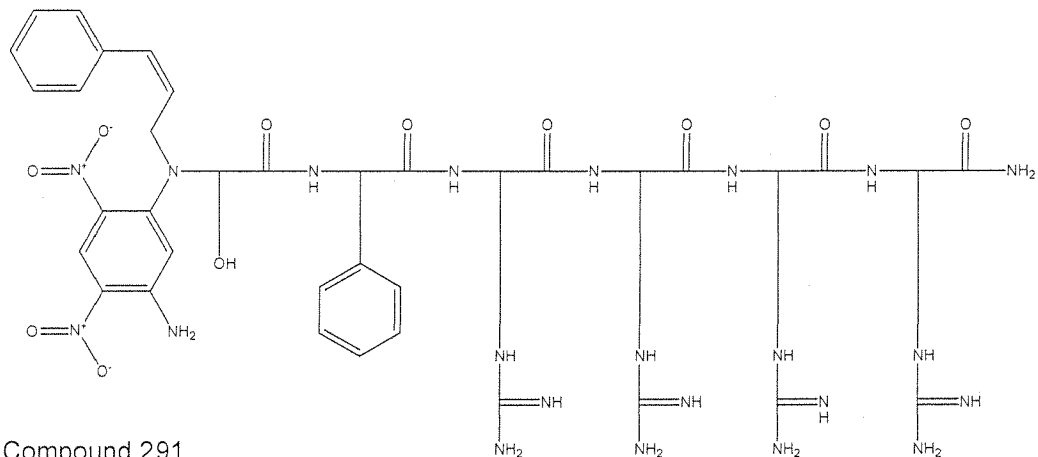
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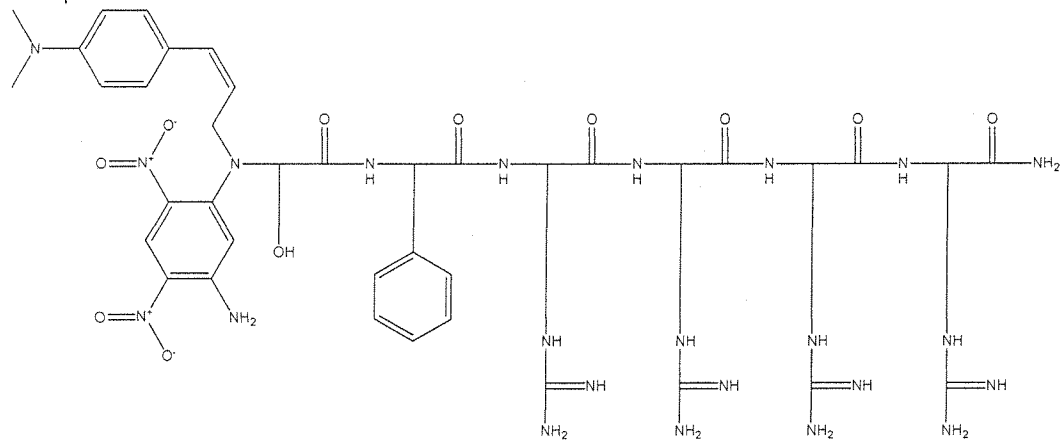
Compound 288

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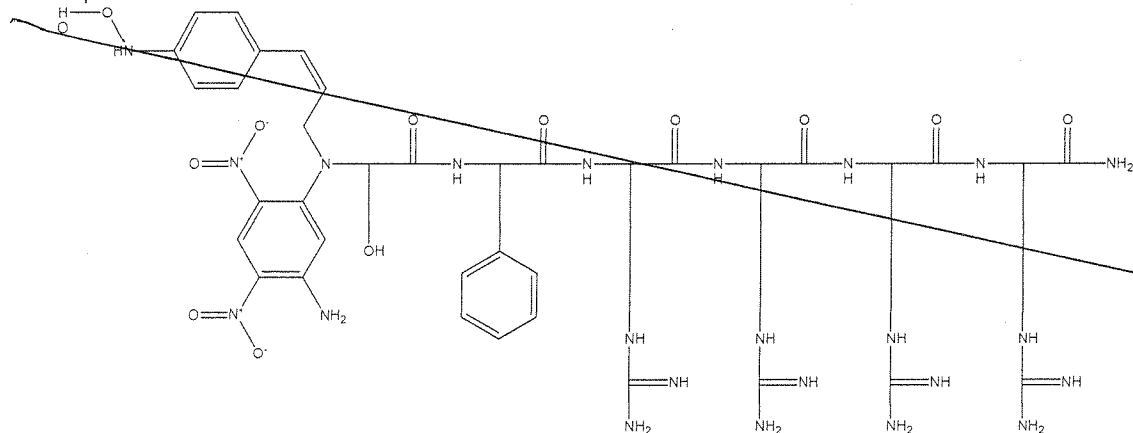




Compound 291

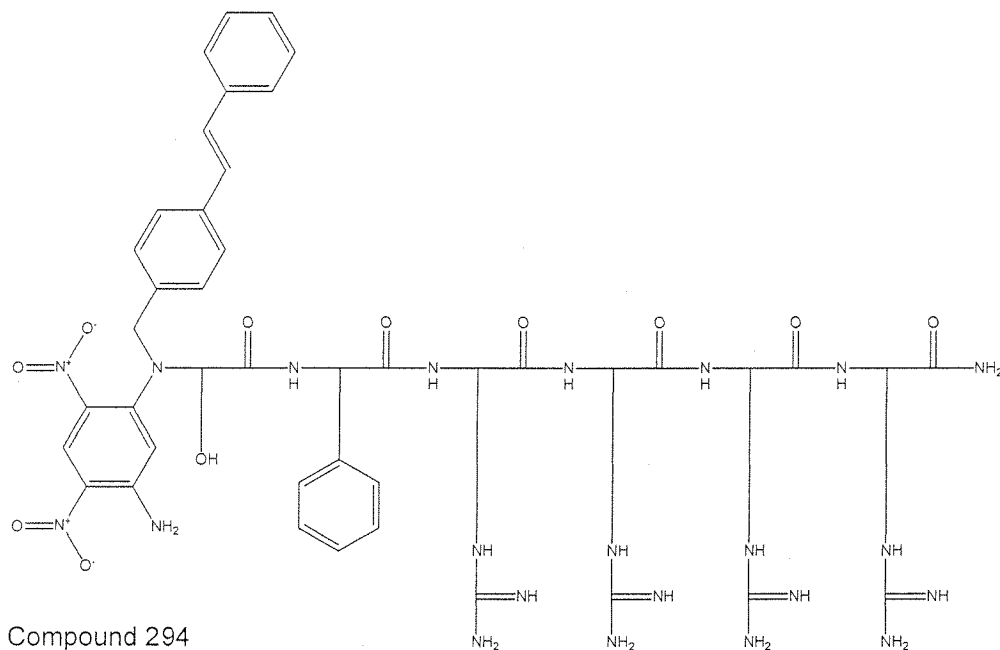


Compound 292

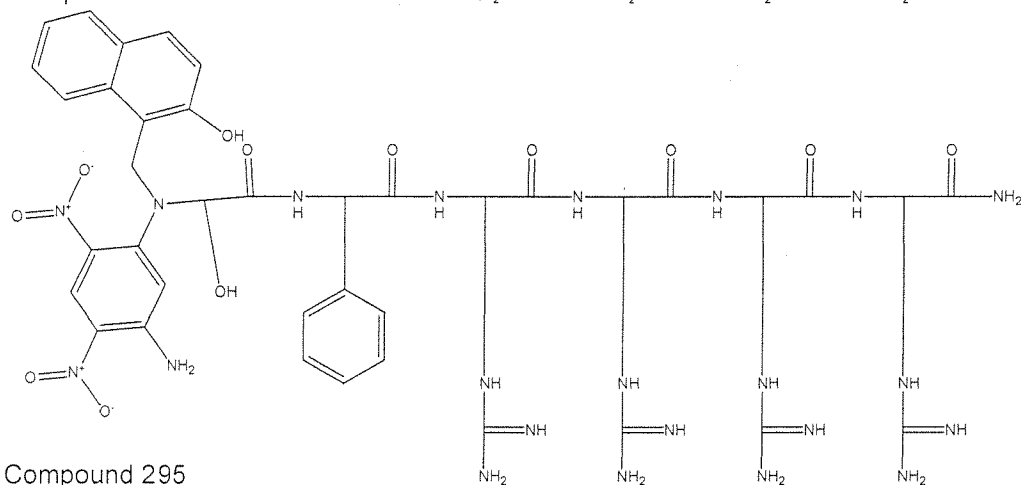


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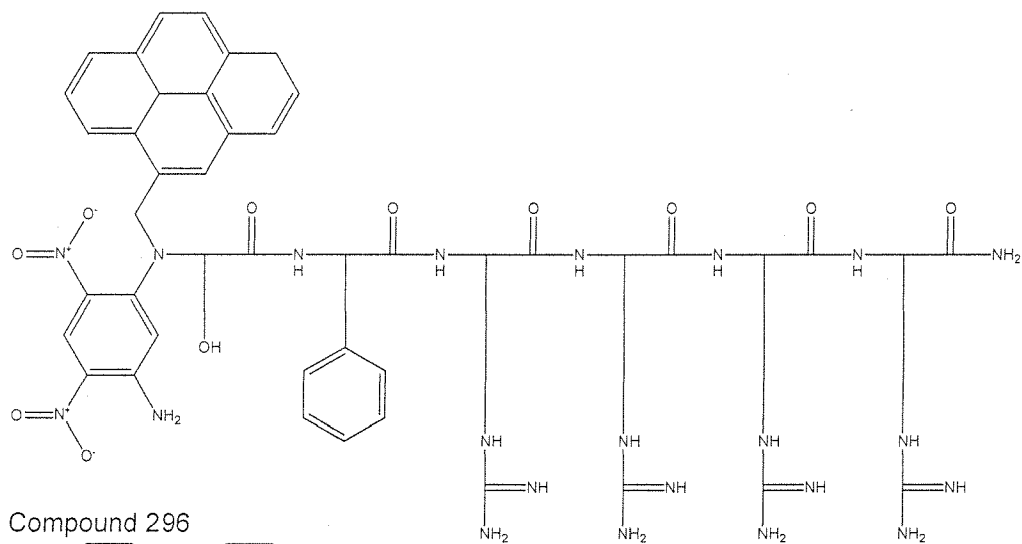


Compound 294

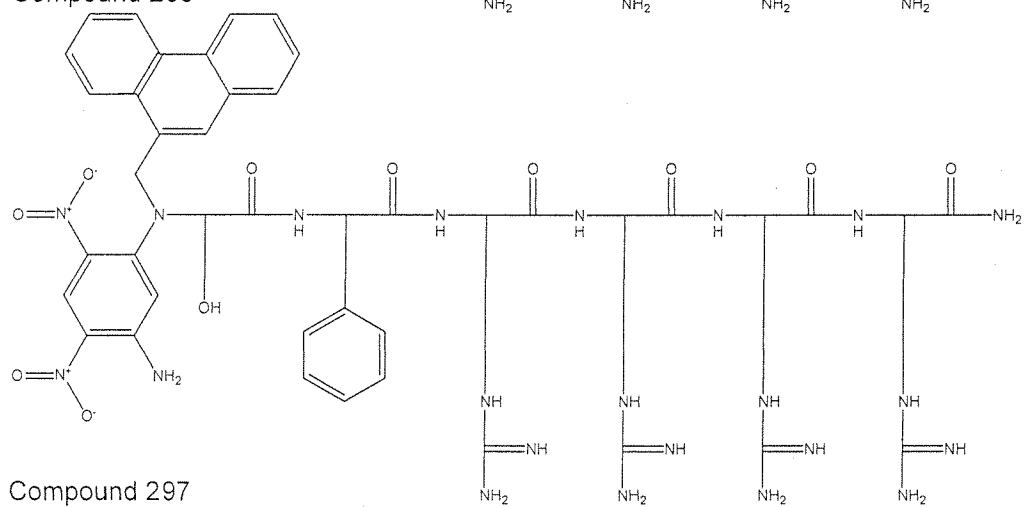


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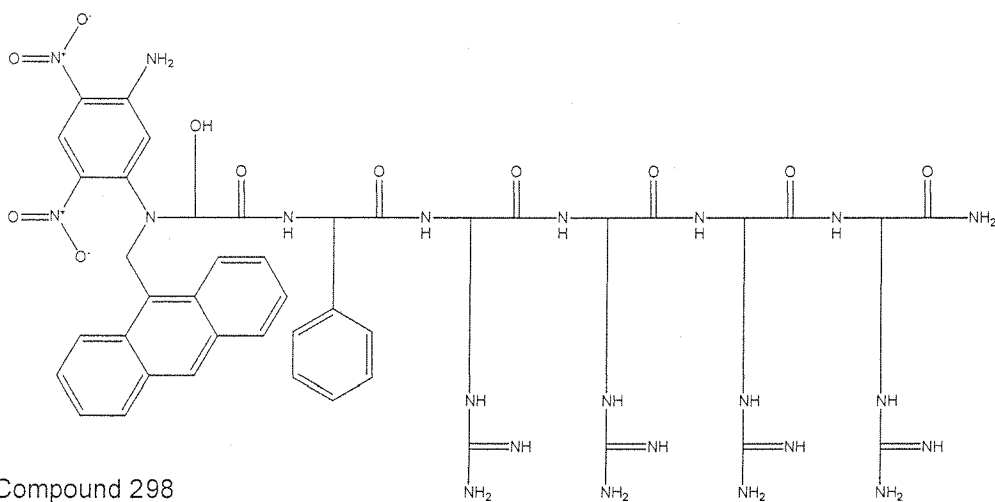


Compound 296

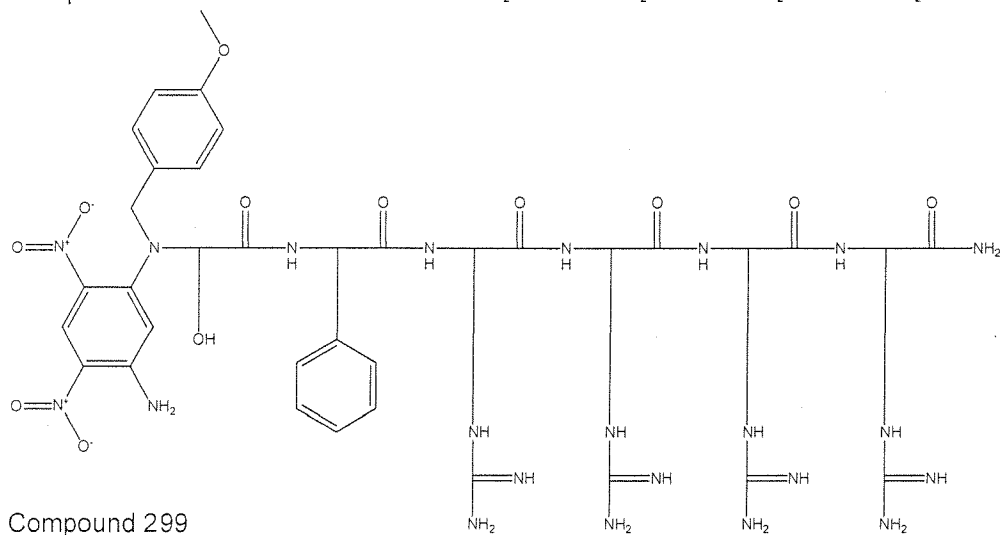


Compound 297

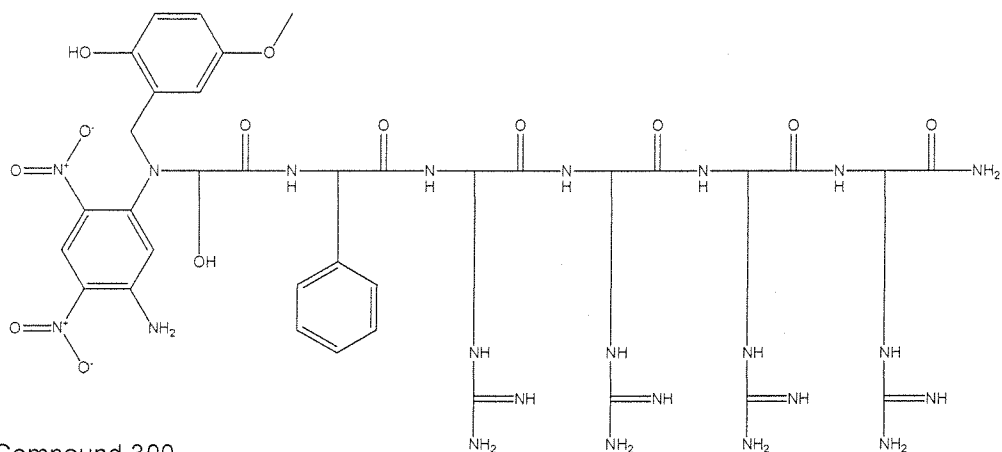
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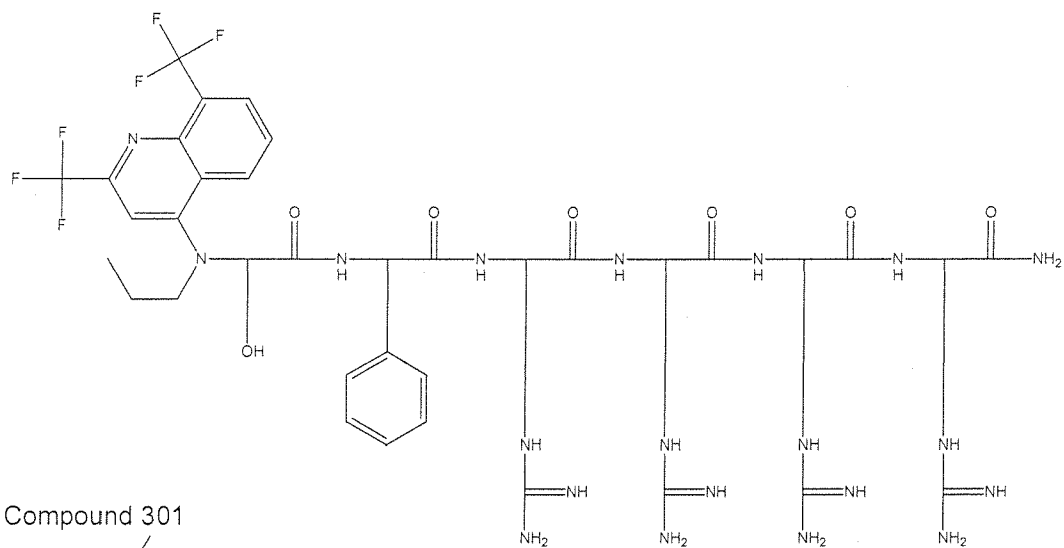
Compound 298



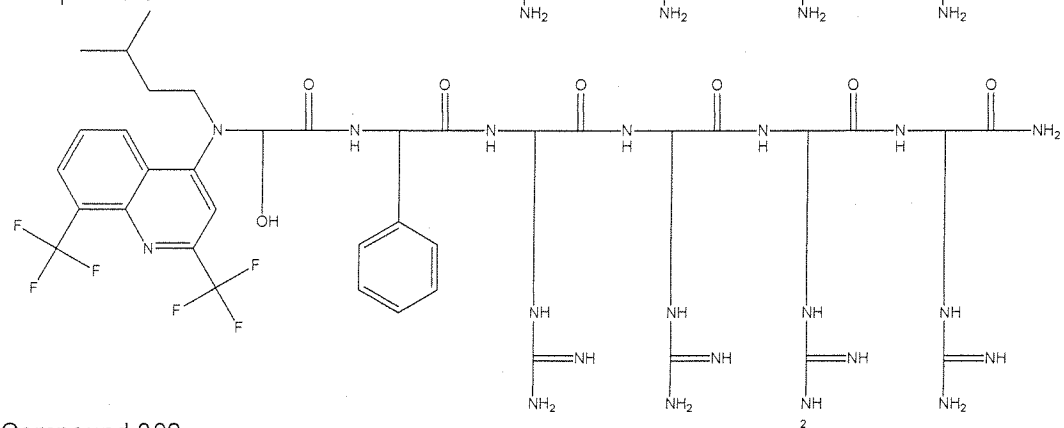
Compound 299



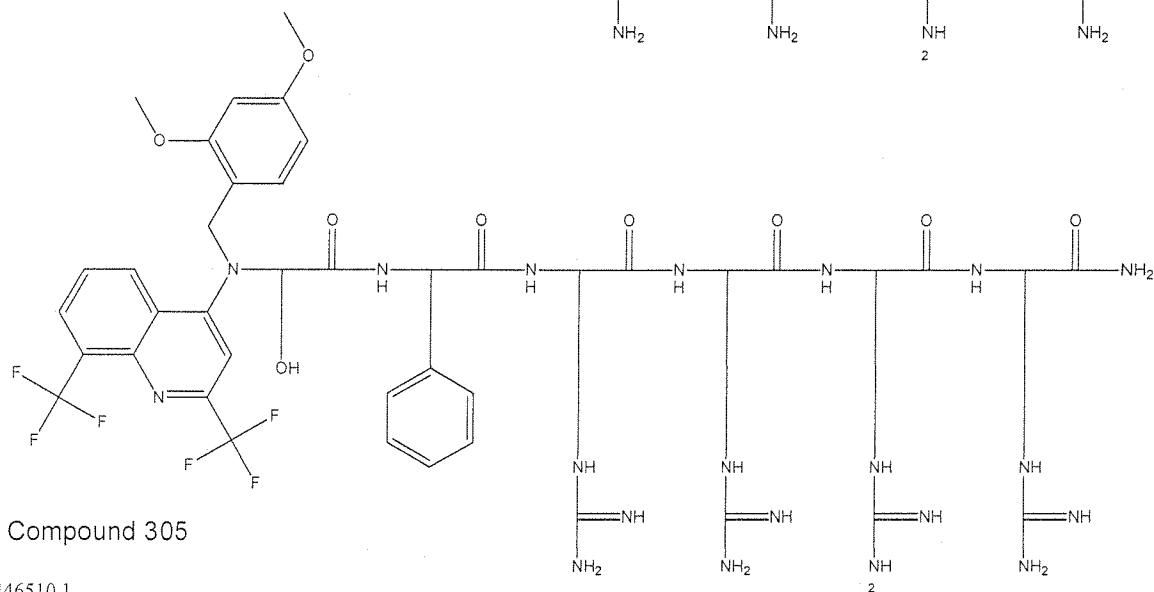
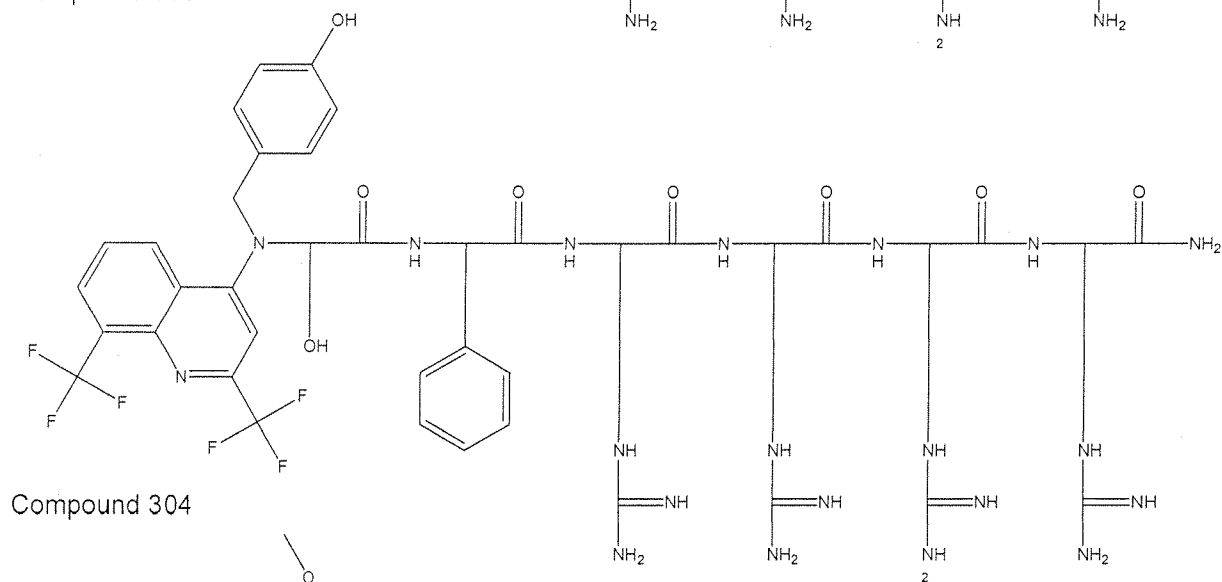
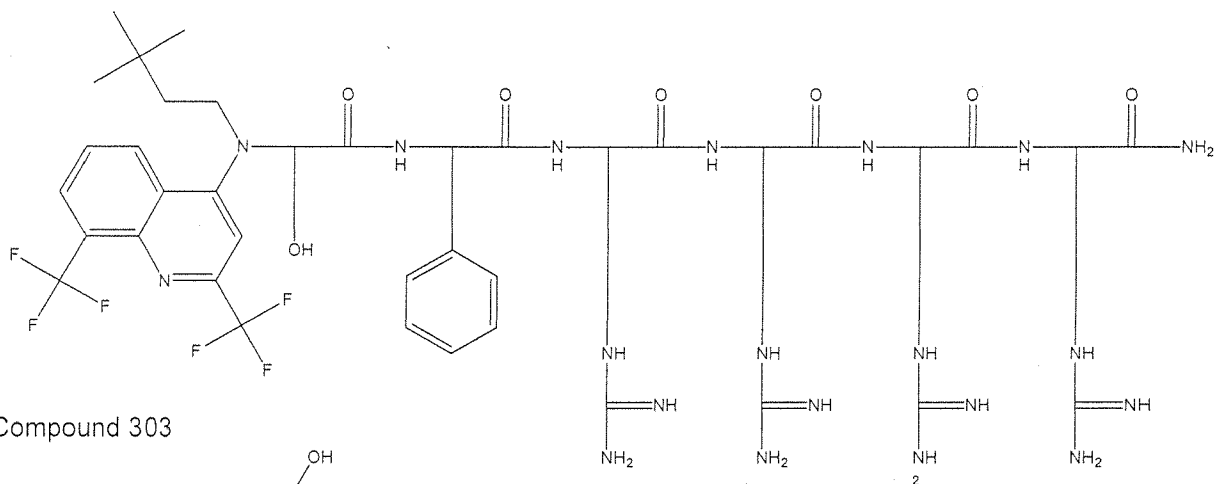
Compound 300

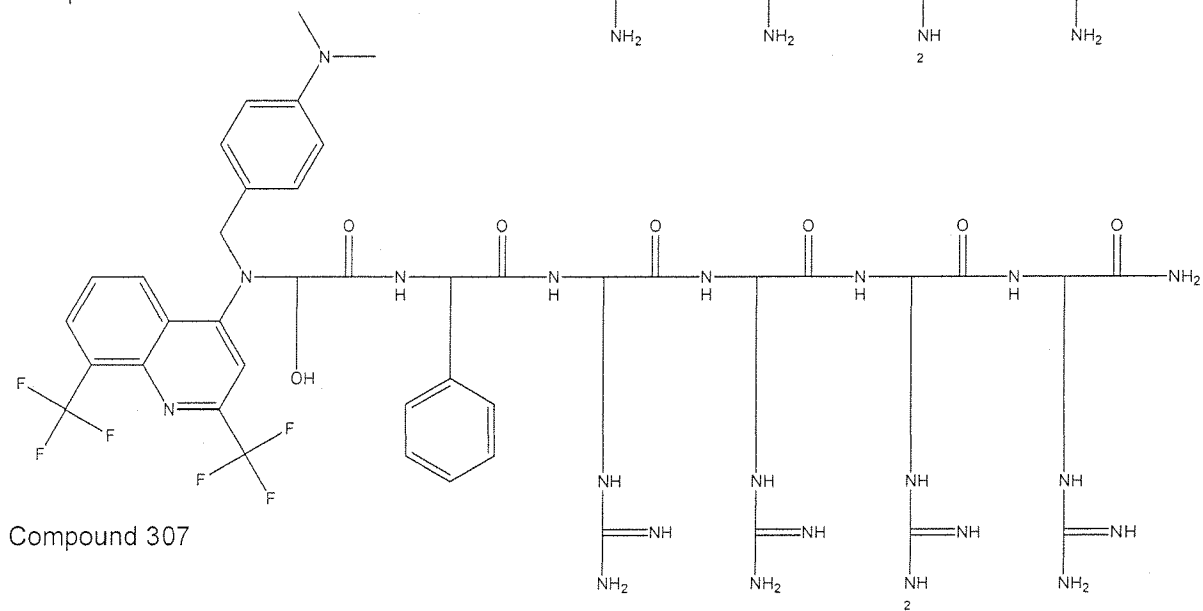
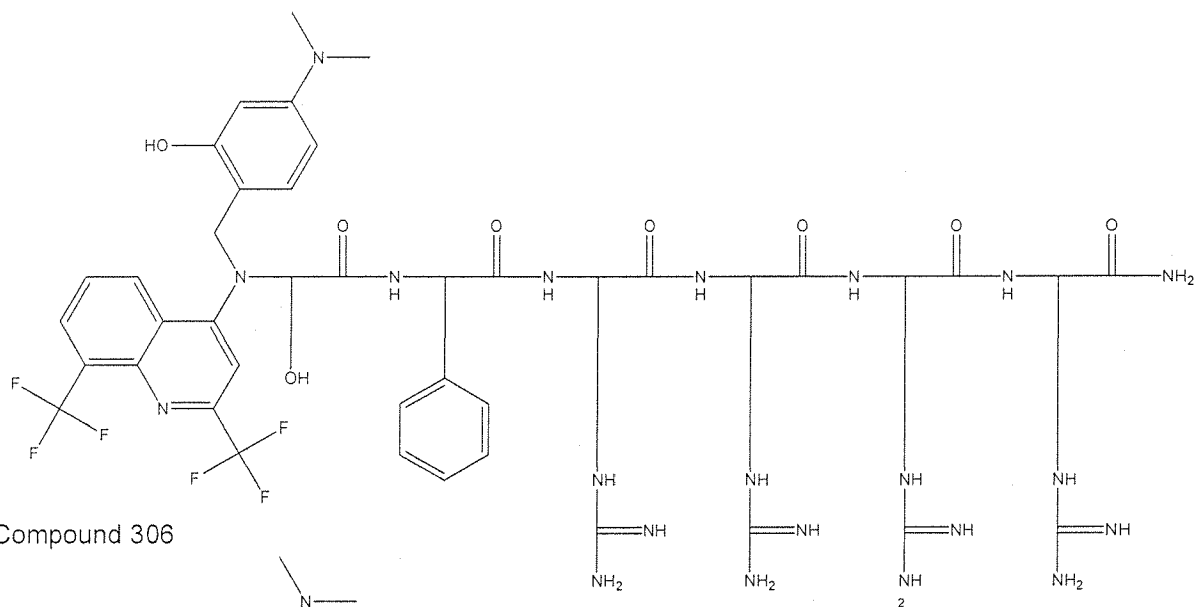


Compound 301

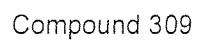
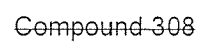


Compound 302

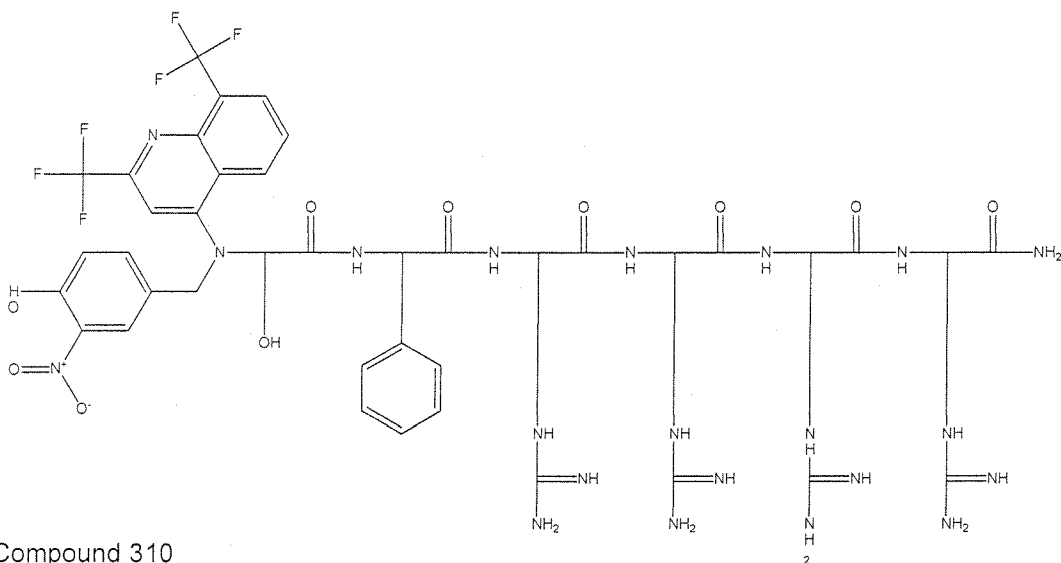




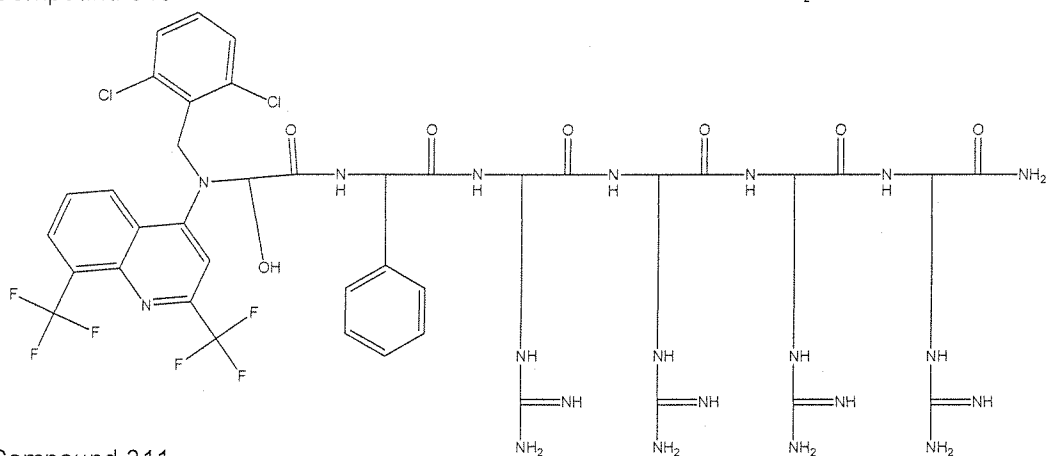
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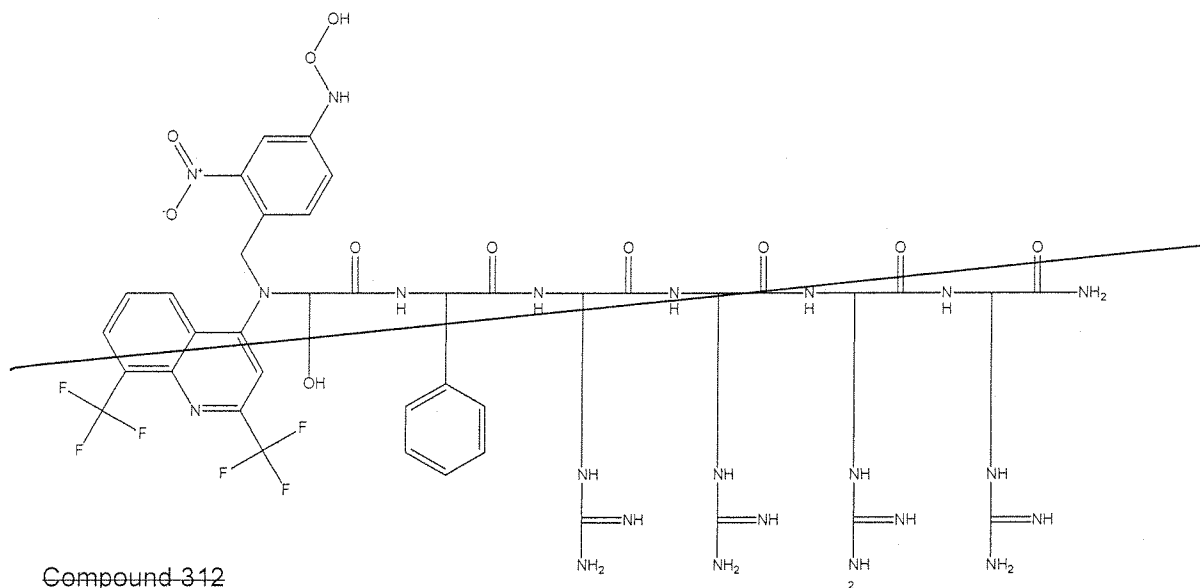


Compound 310

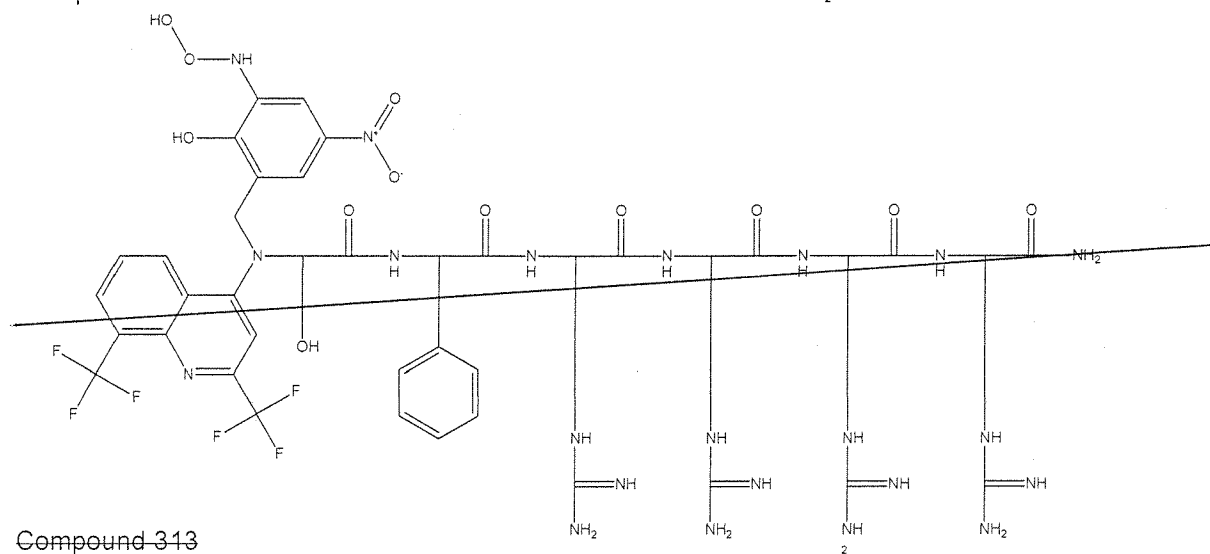


Compound 311

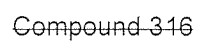
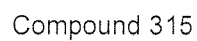
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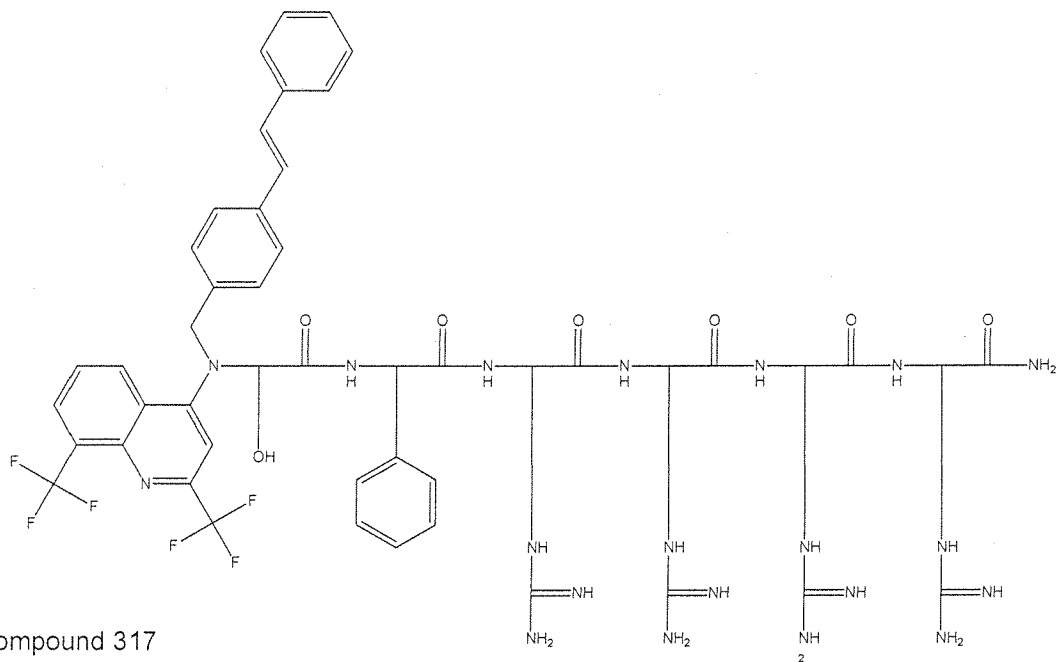
~~Compound 312~~

~~Compound 313~~

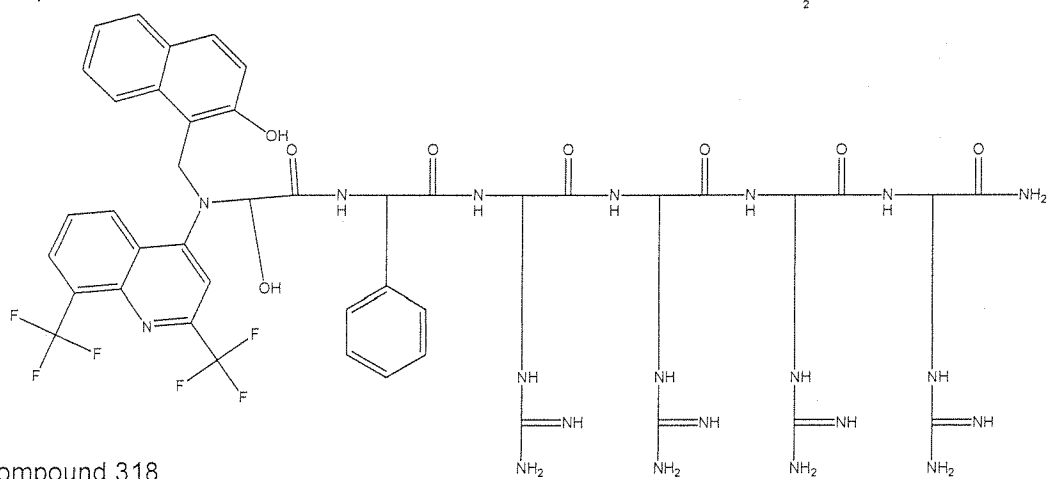
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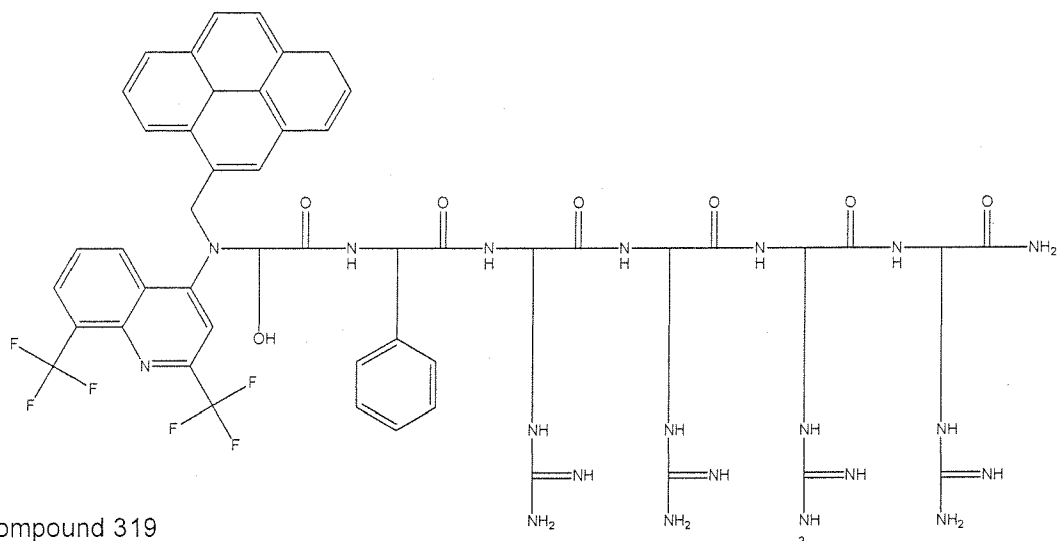


Compound 317

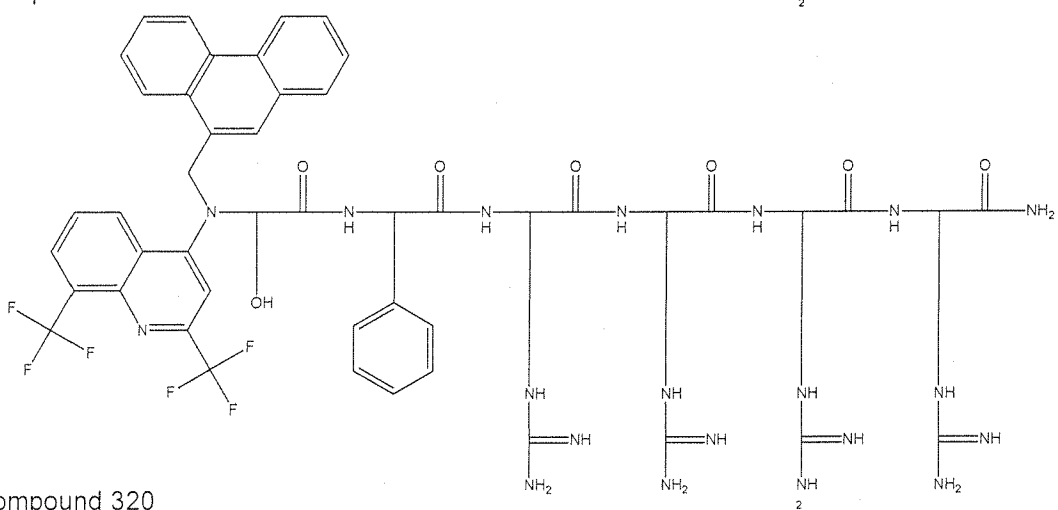


Compound 318

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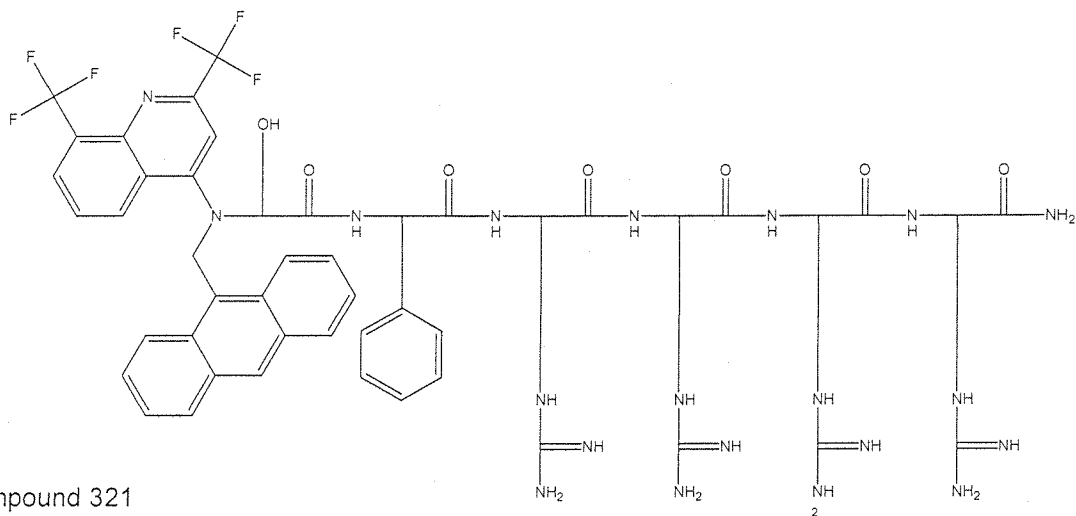


Compound 319

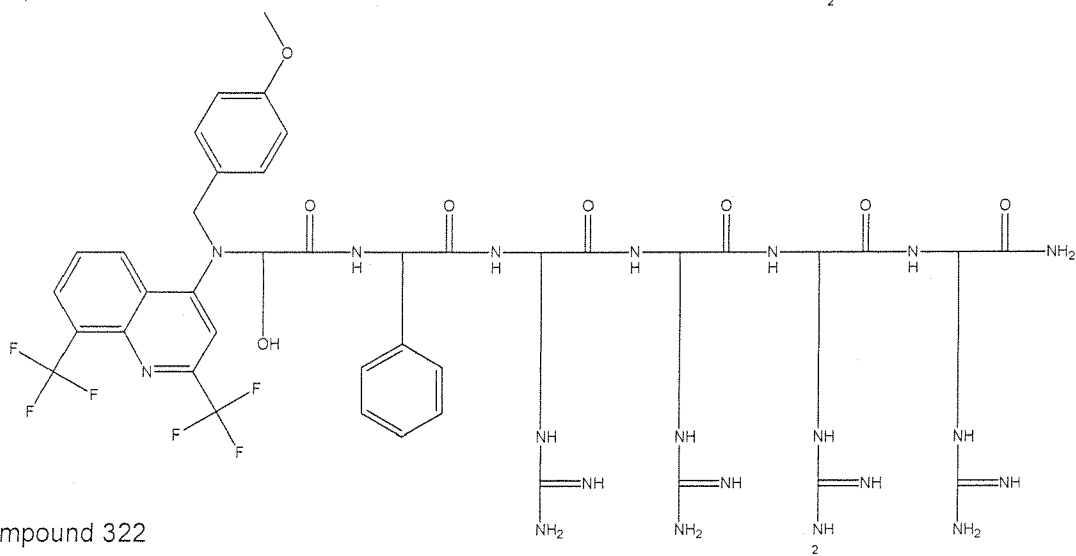


Compound 320

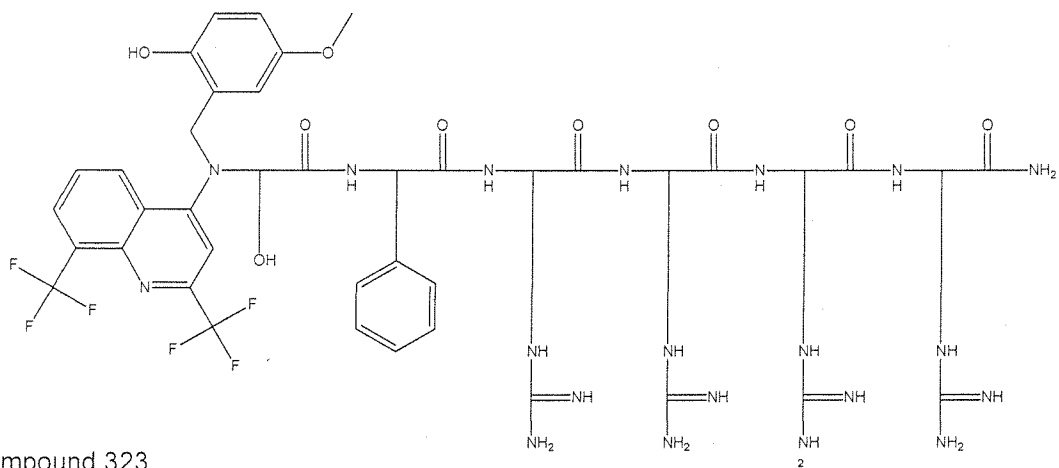
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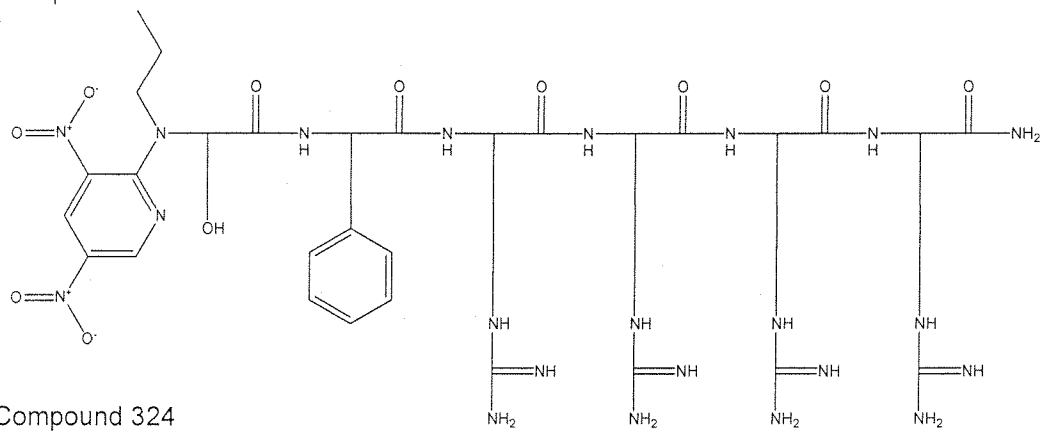
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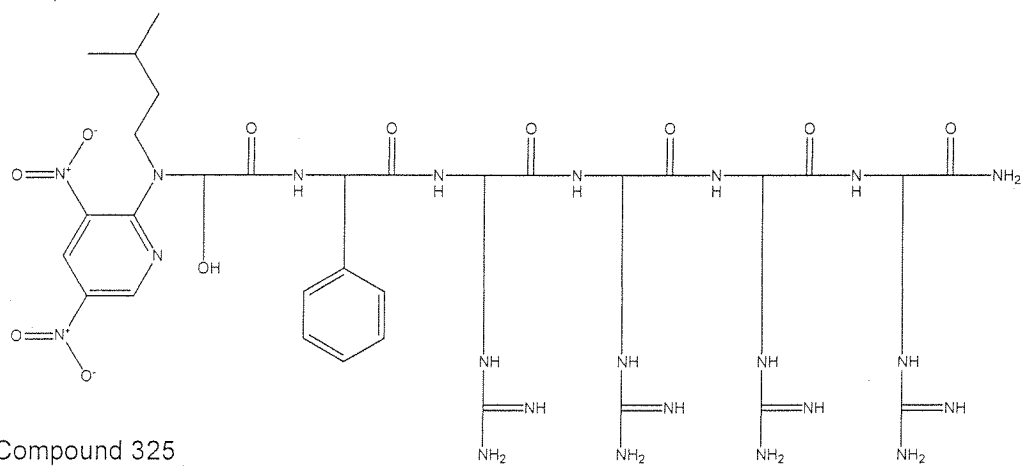
Compound 322



Compound 323

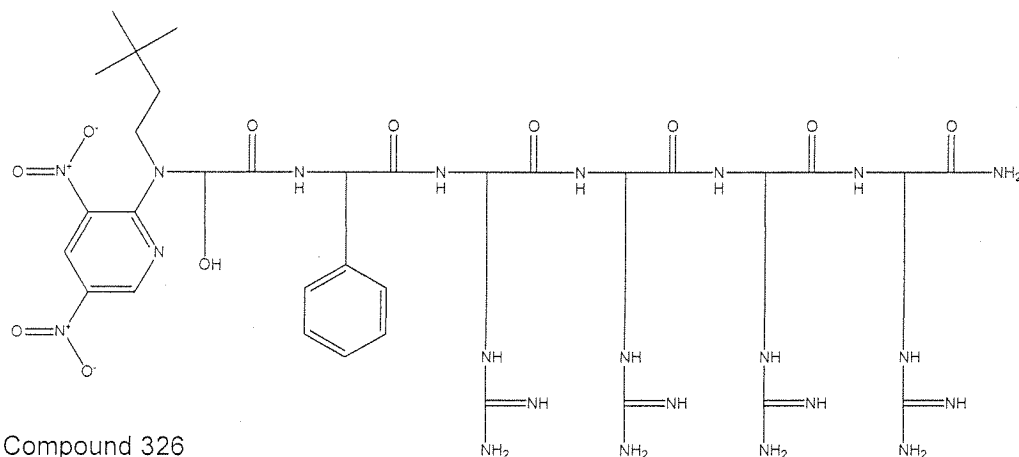


Compound 324

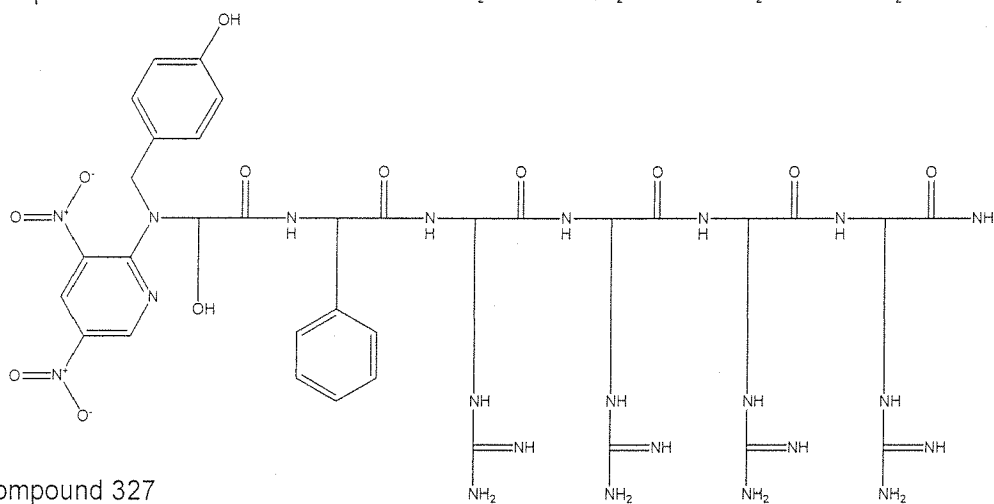


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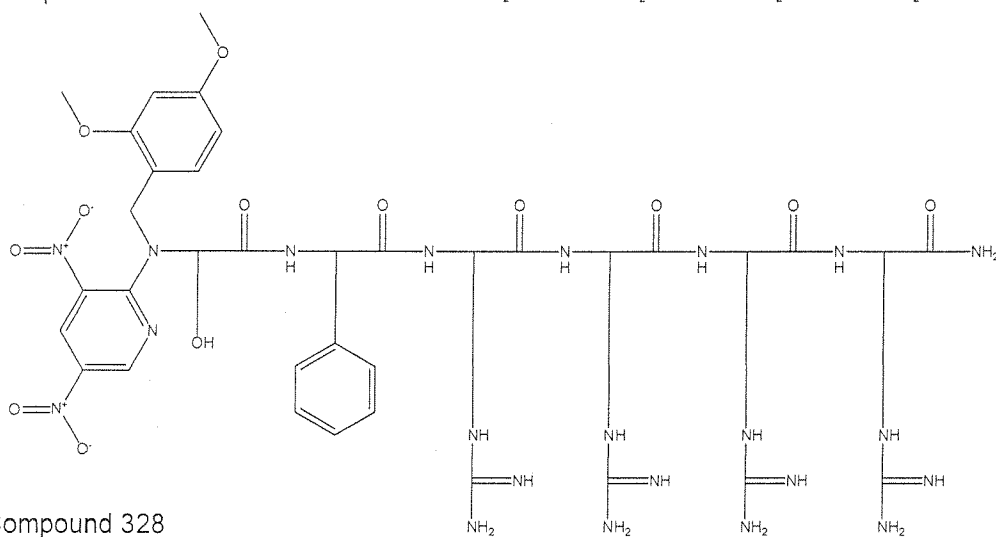
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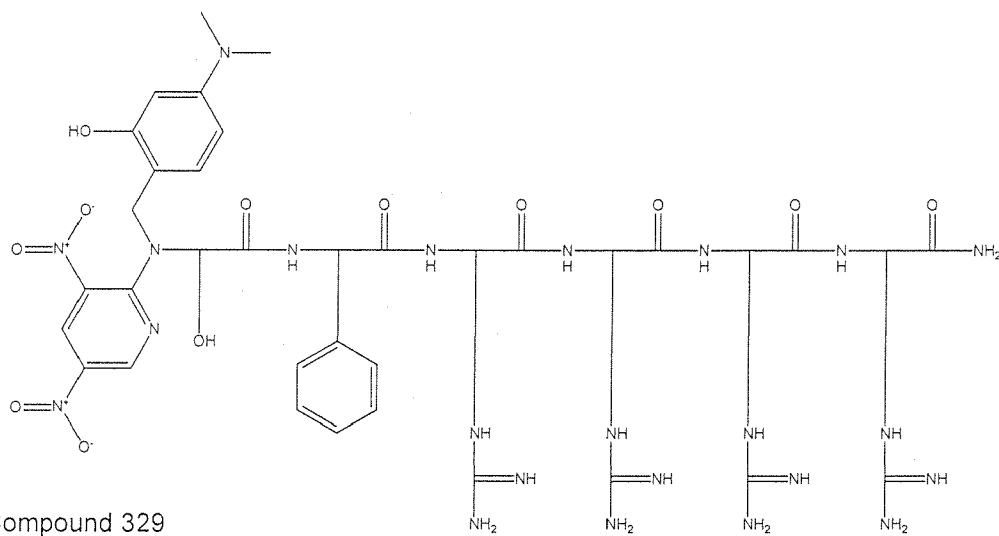
Compound 326



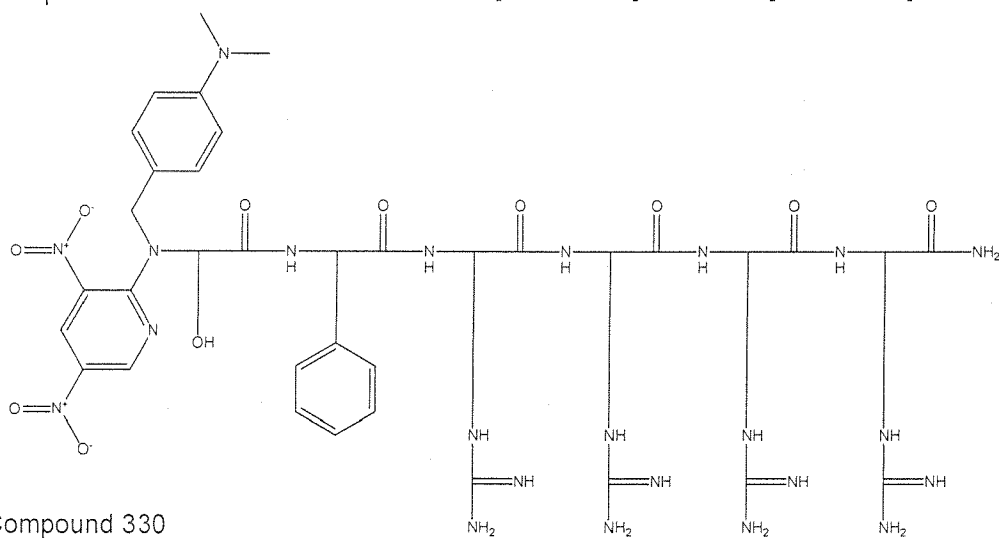
Compound 327



Compound 328

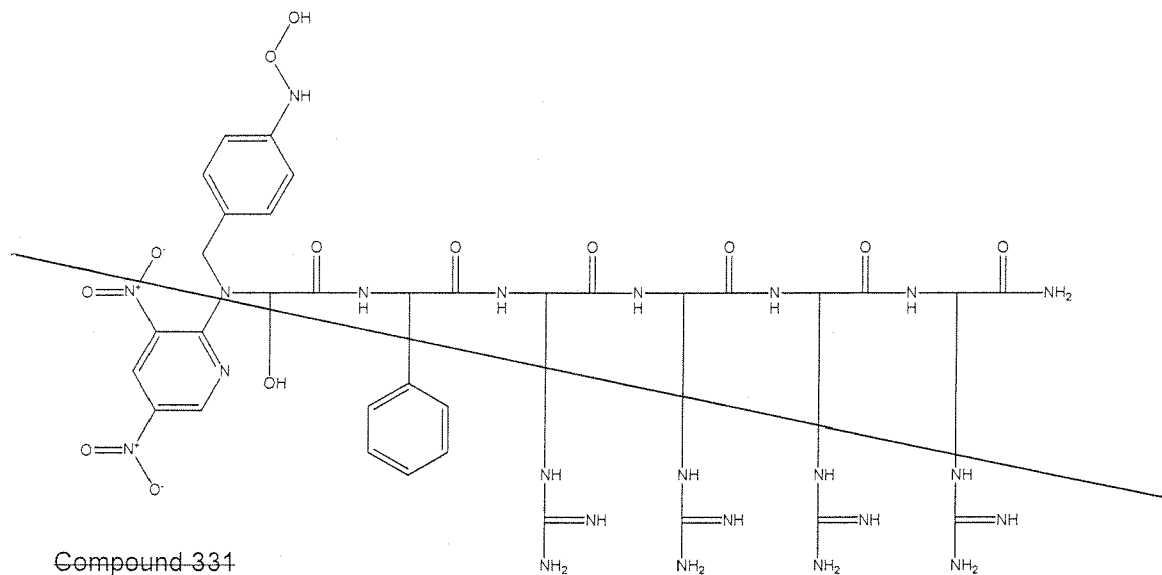


Compound 329

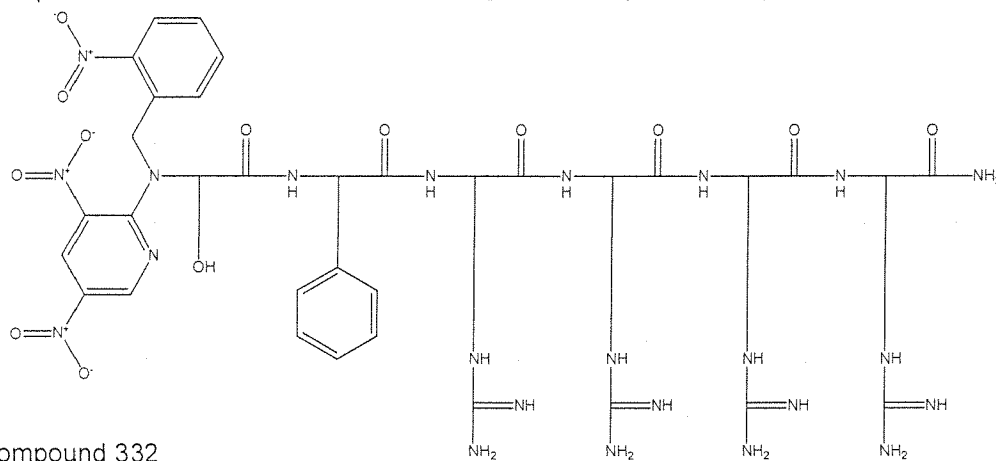


Compound 330

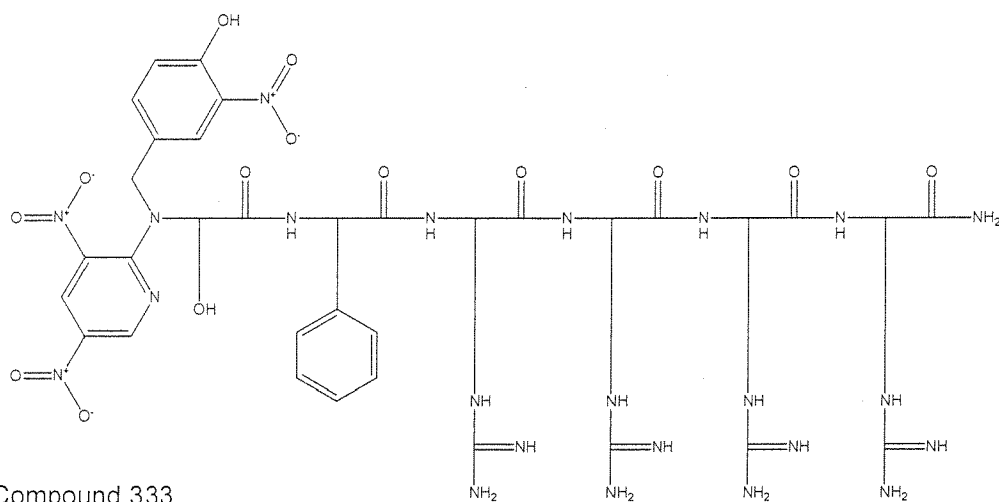
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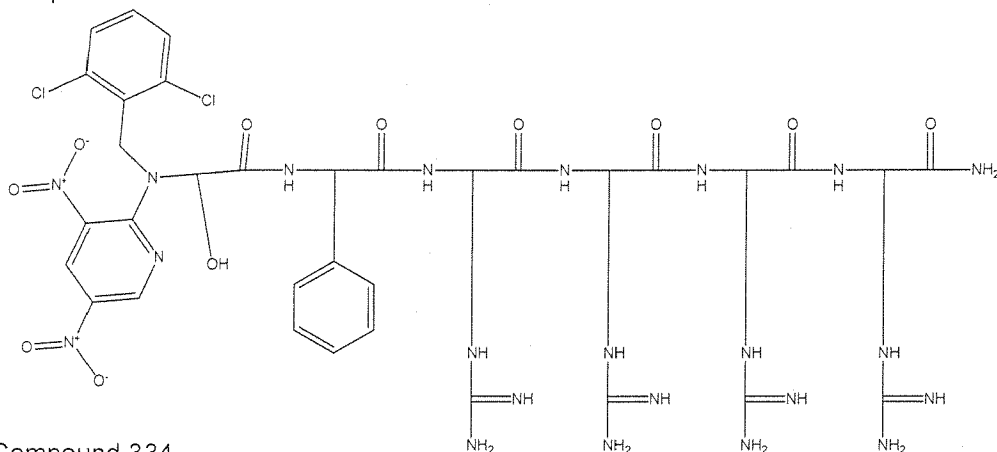
Compound 331



Compound 332

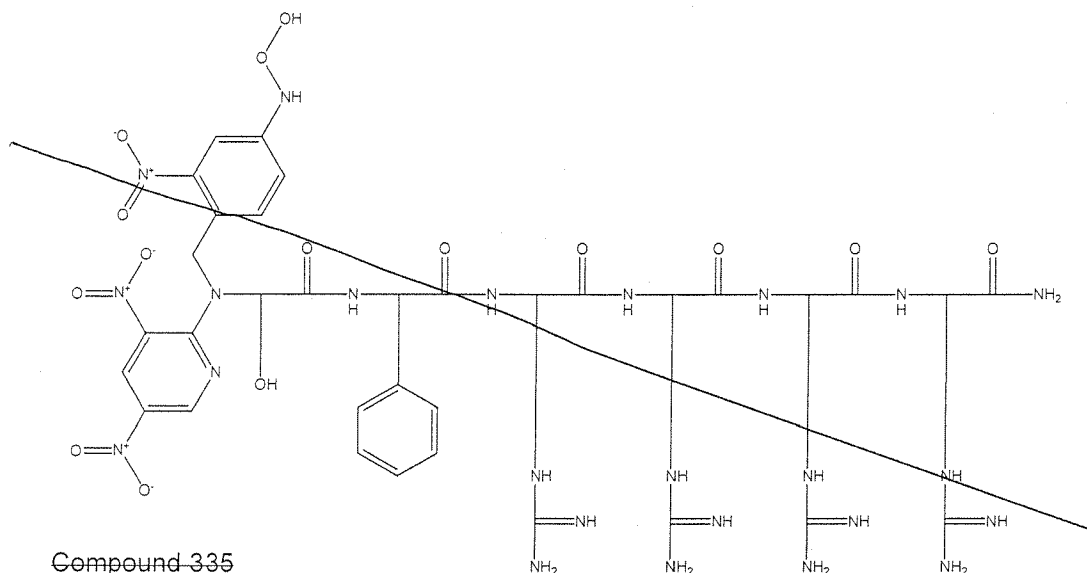


Compound 333

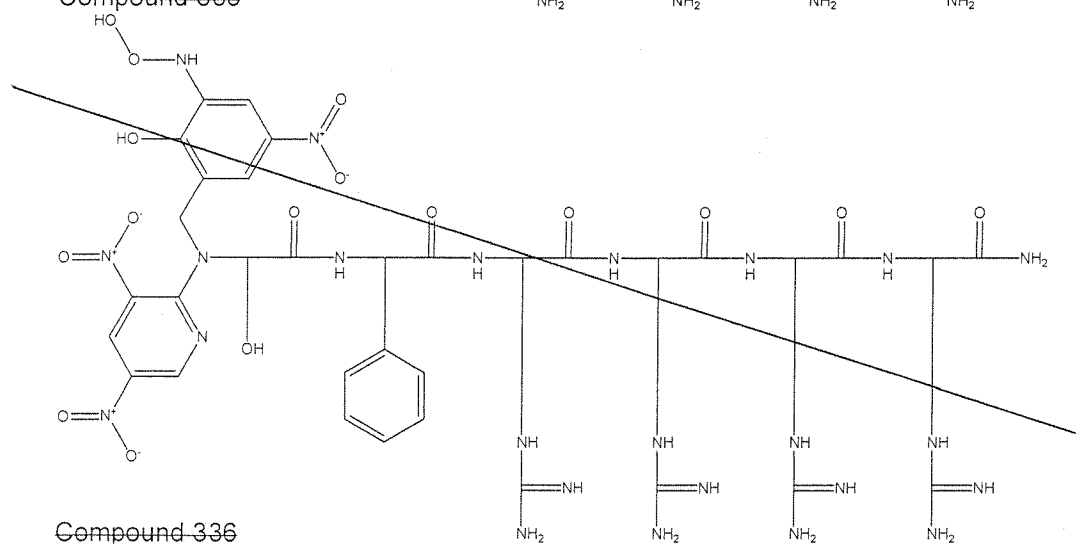


Compound 334

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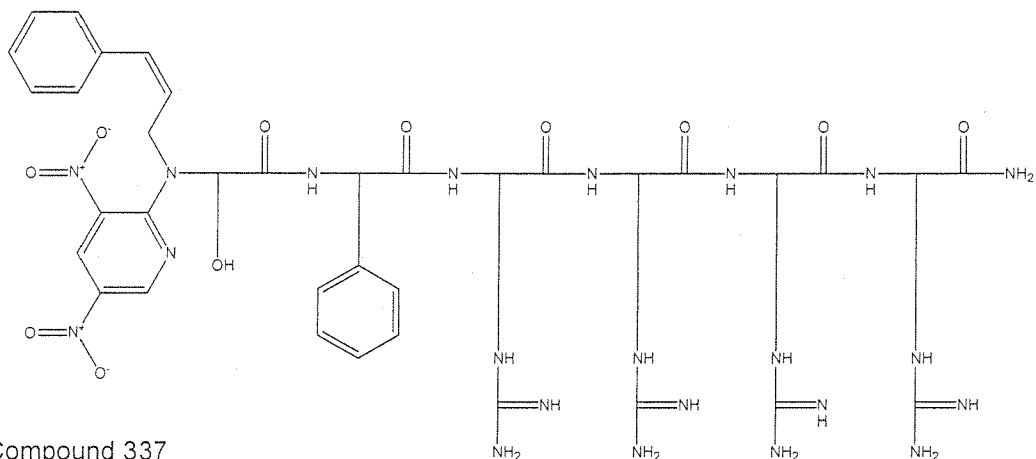


Compound 335

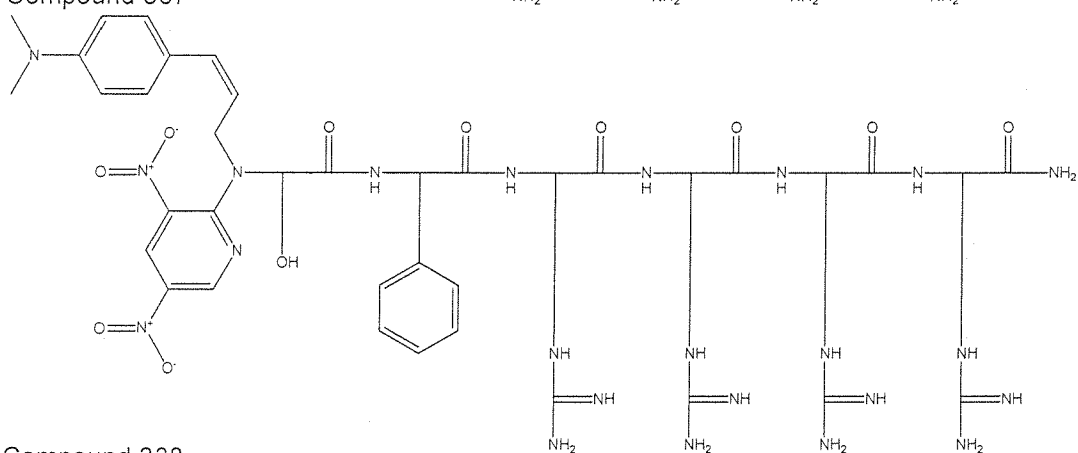


Compound 336

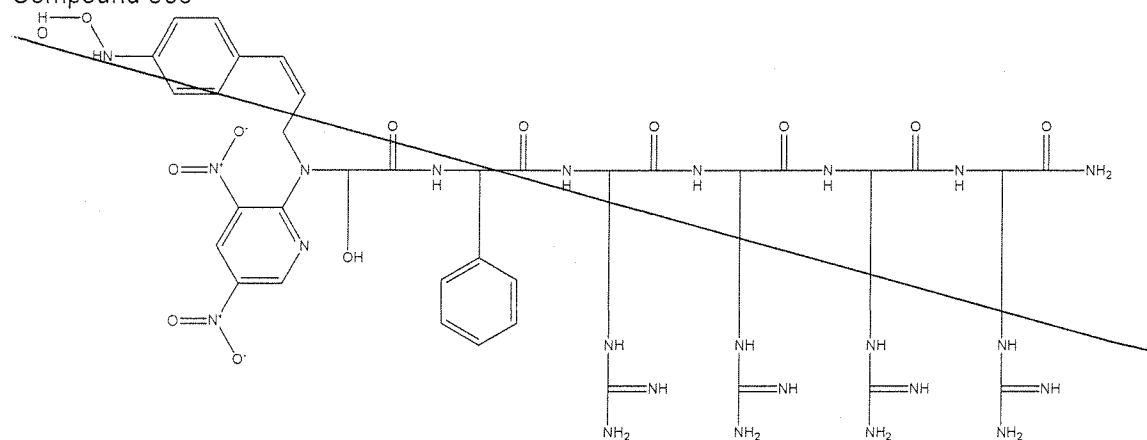
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Compound 337

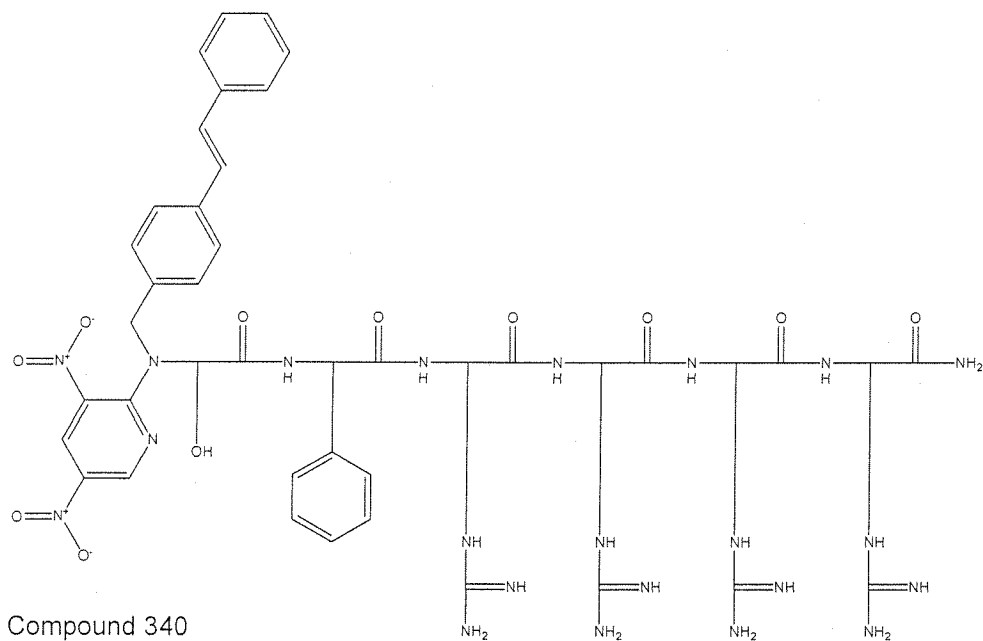


Compound 338

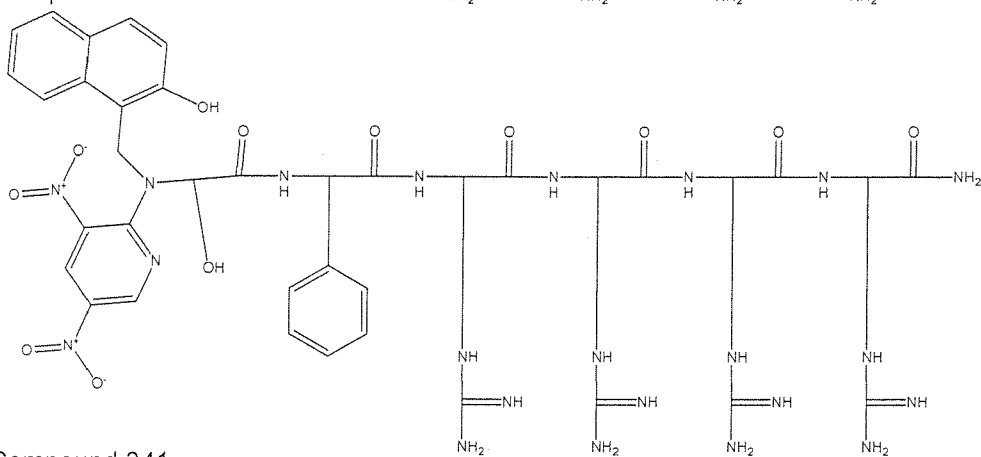


Compound 339

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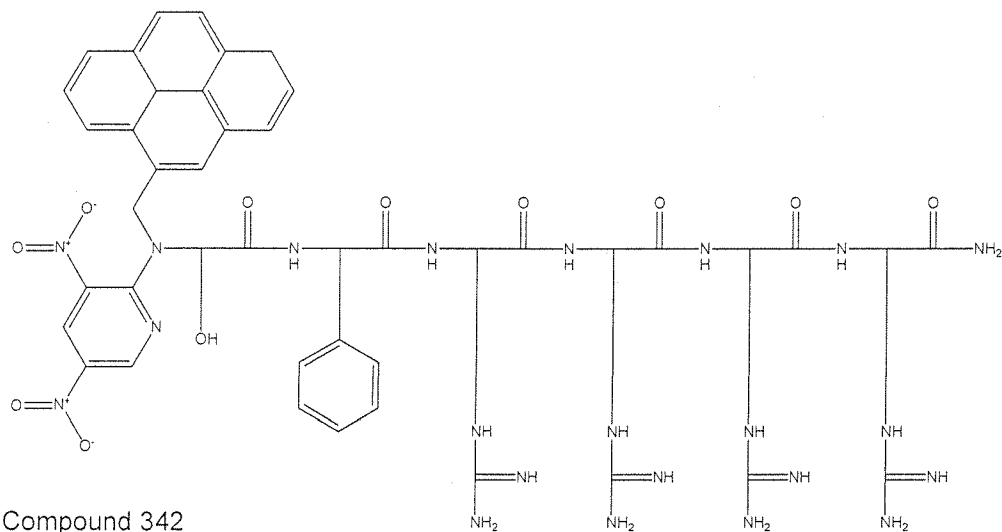


Compound 340

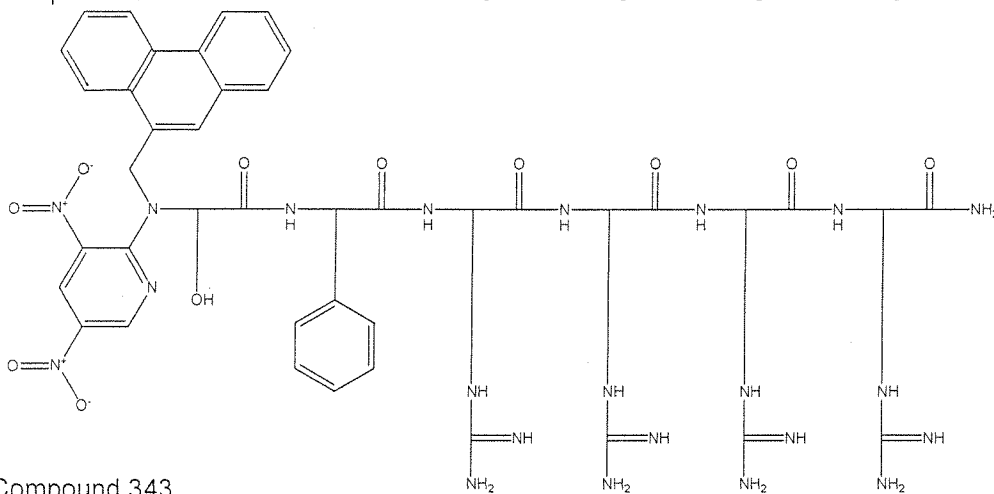


Compound 341

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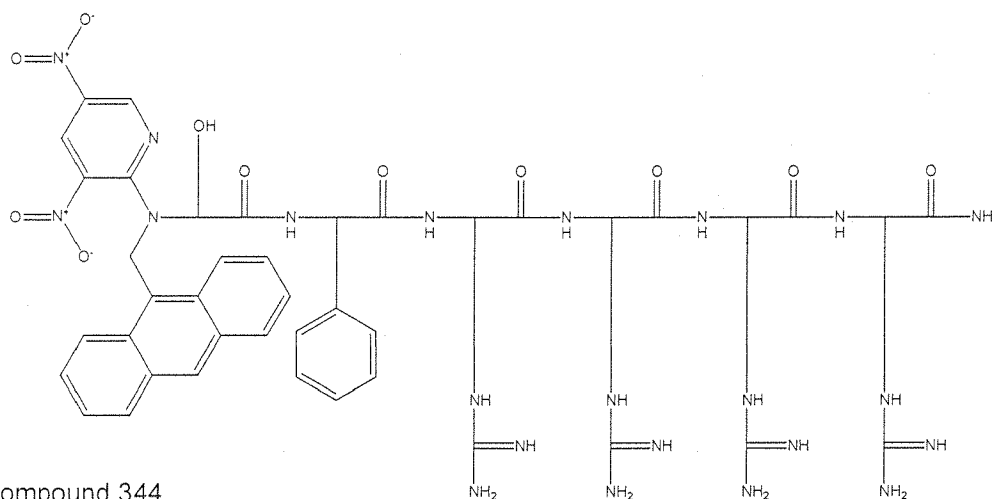


Compound 342

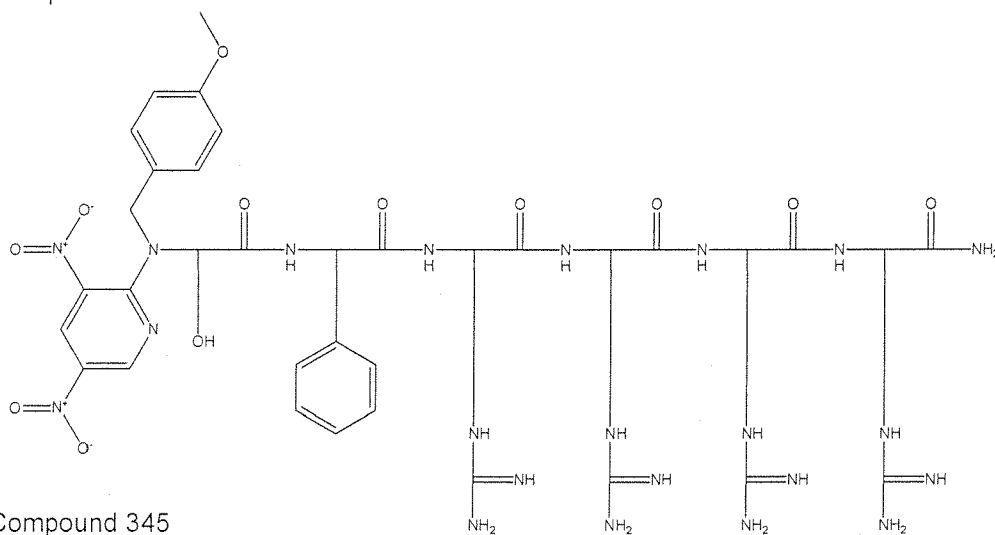


Compound 343

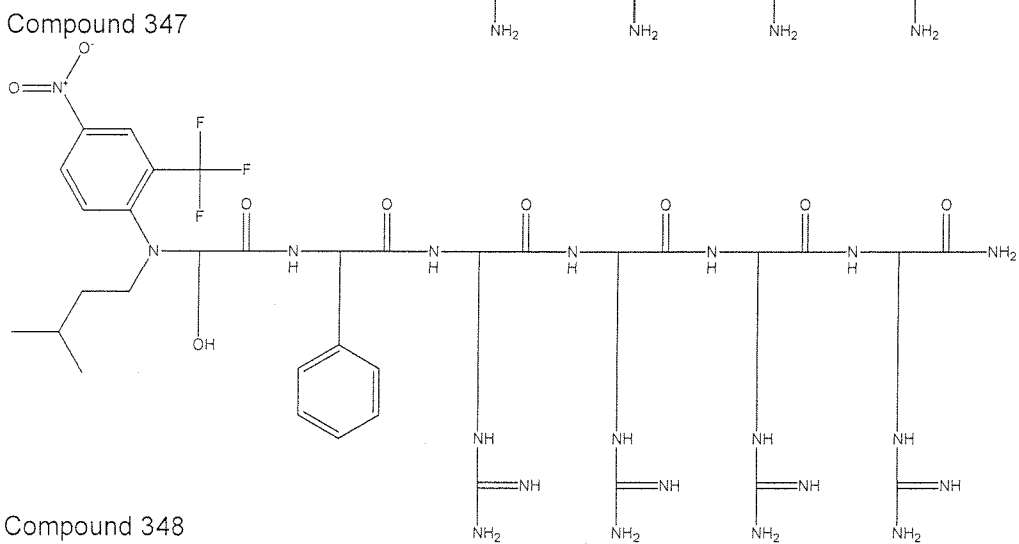
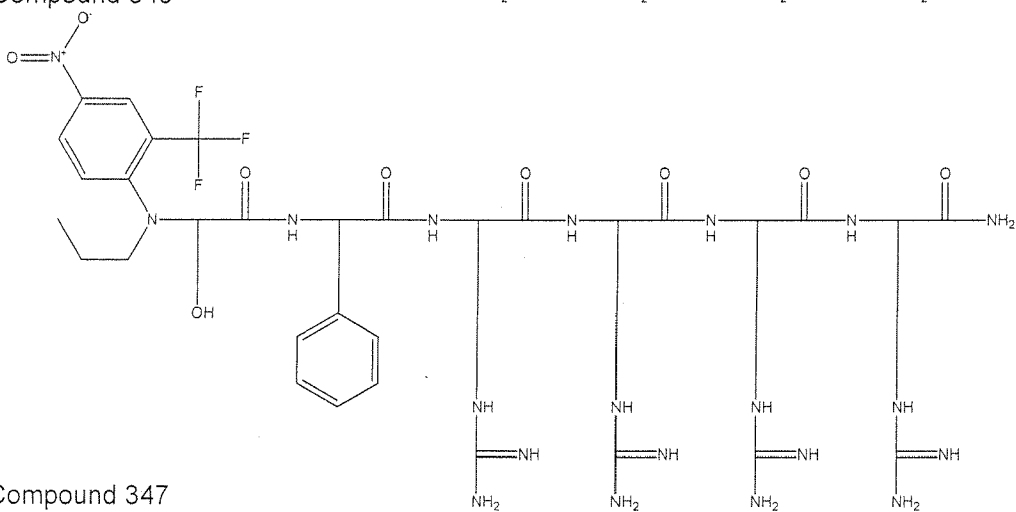
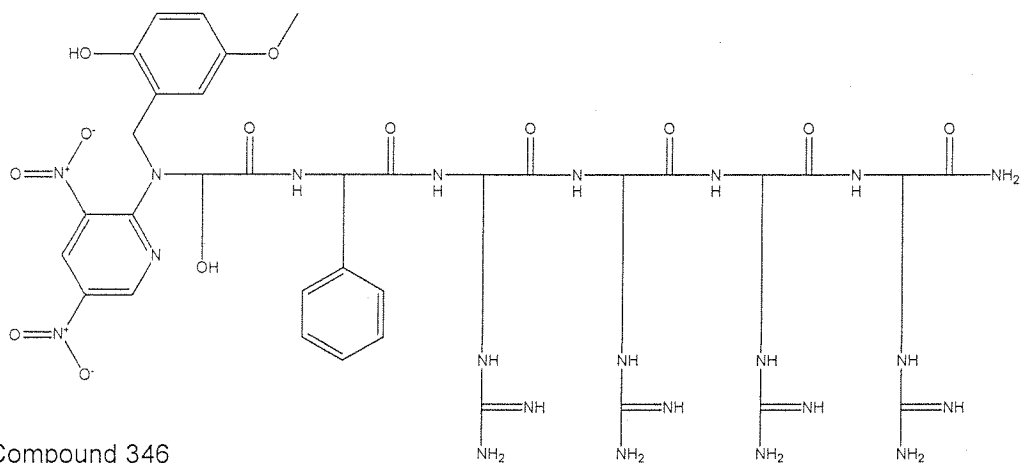
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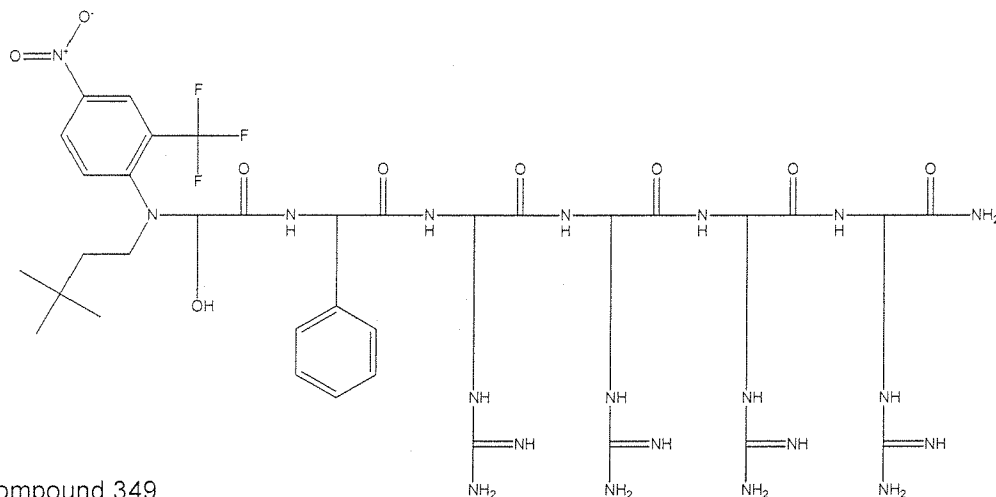
Compound 344



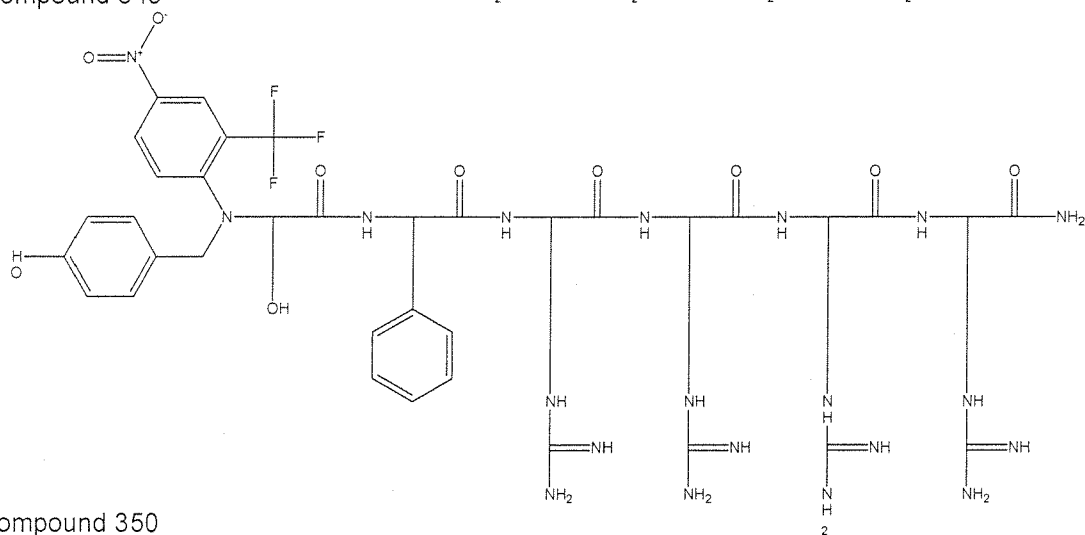
Compound 345



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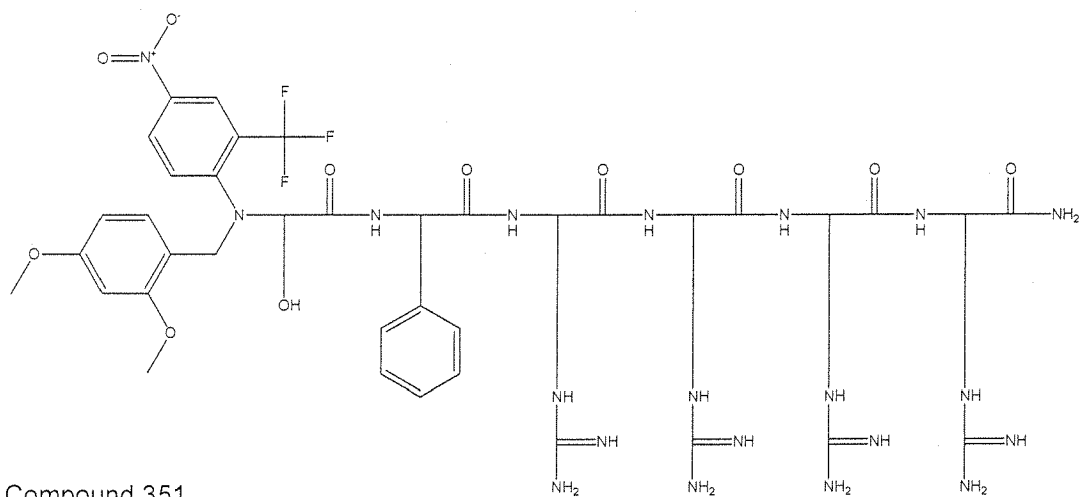


Compound 349

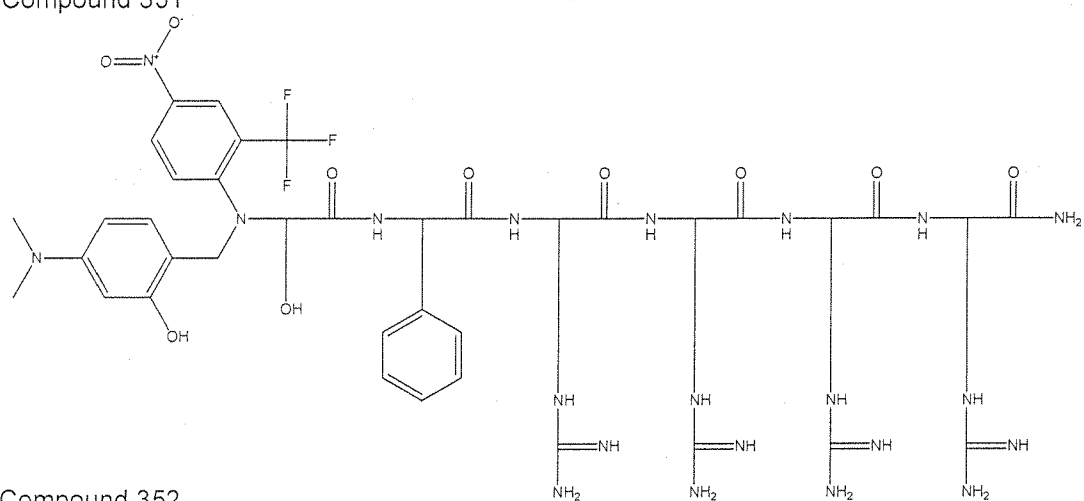


Compound 350

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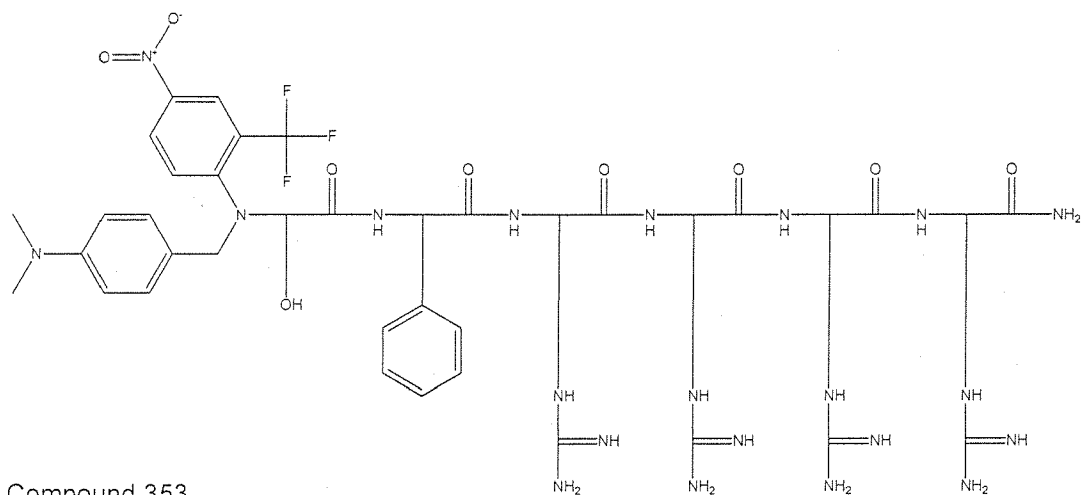


Compound 351

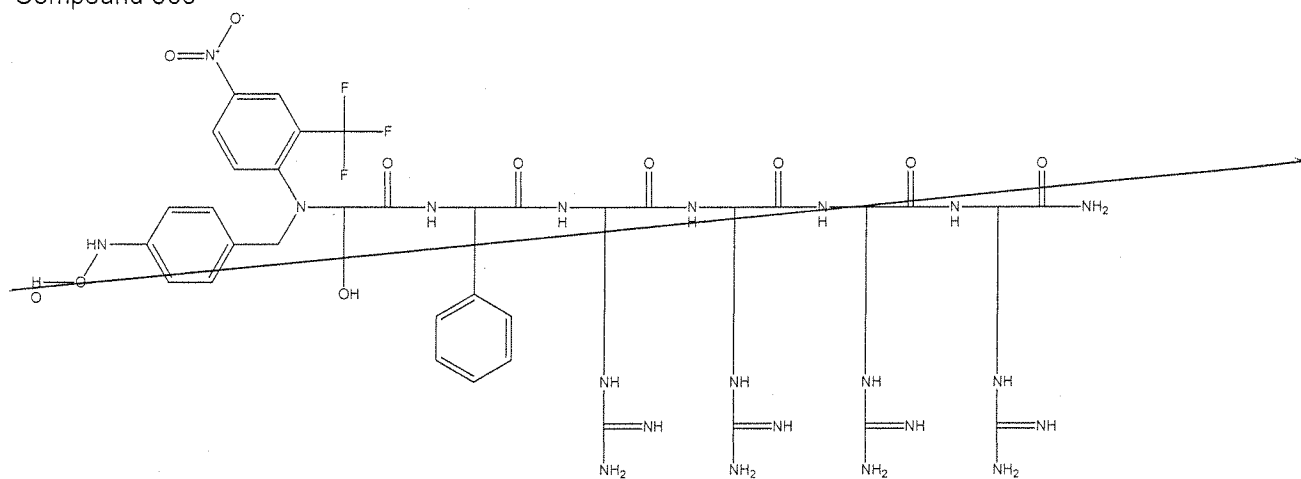


Compound 352

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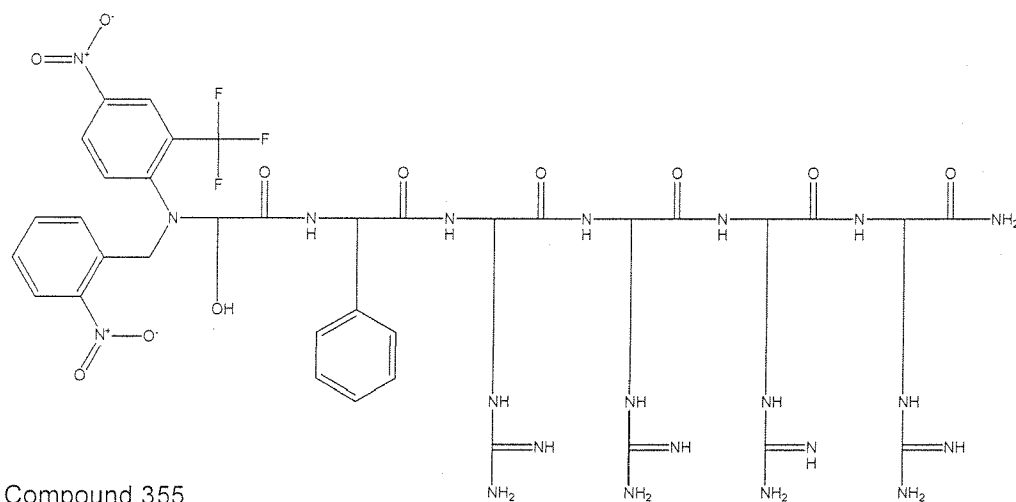


Compound 353

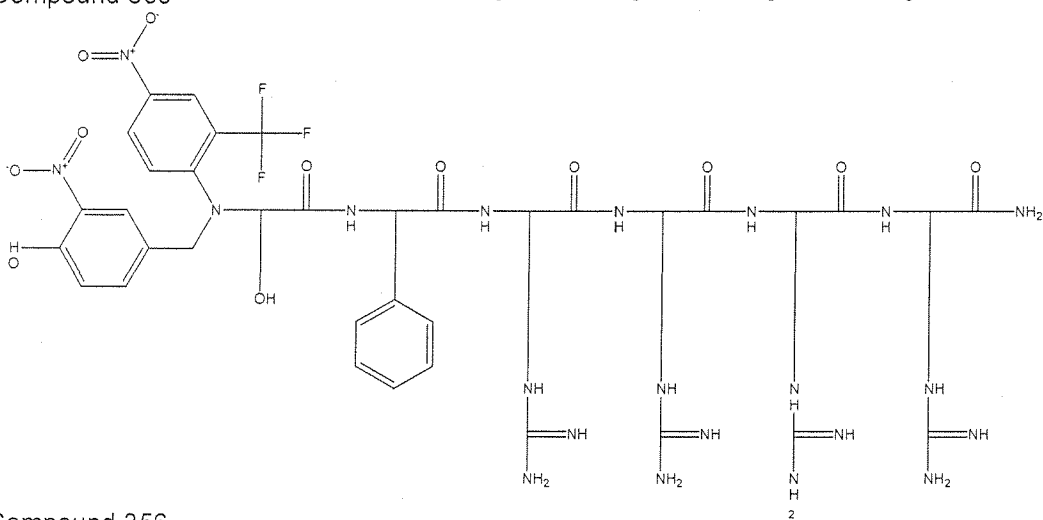


Compound 354

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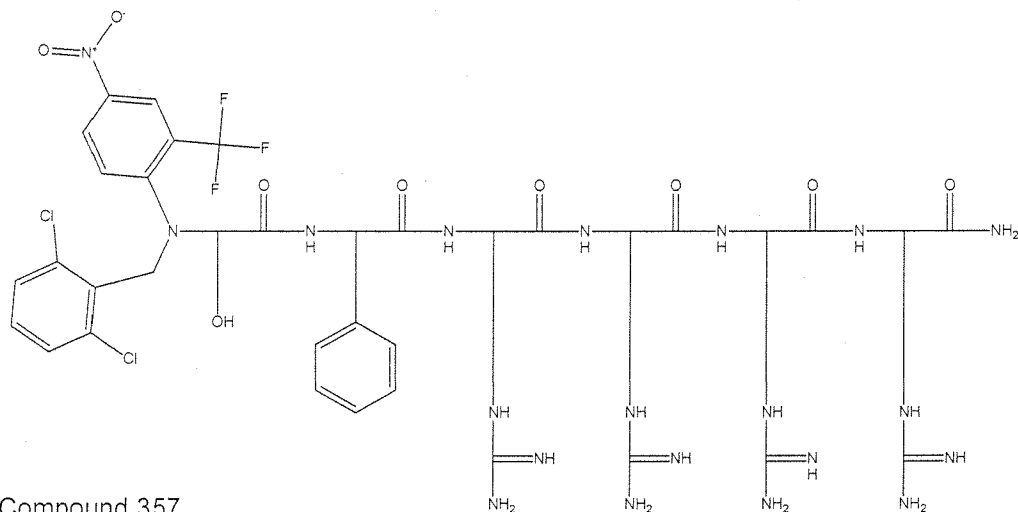


Compound 355

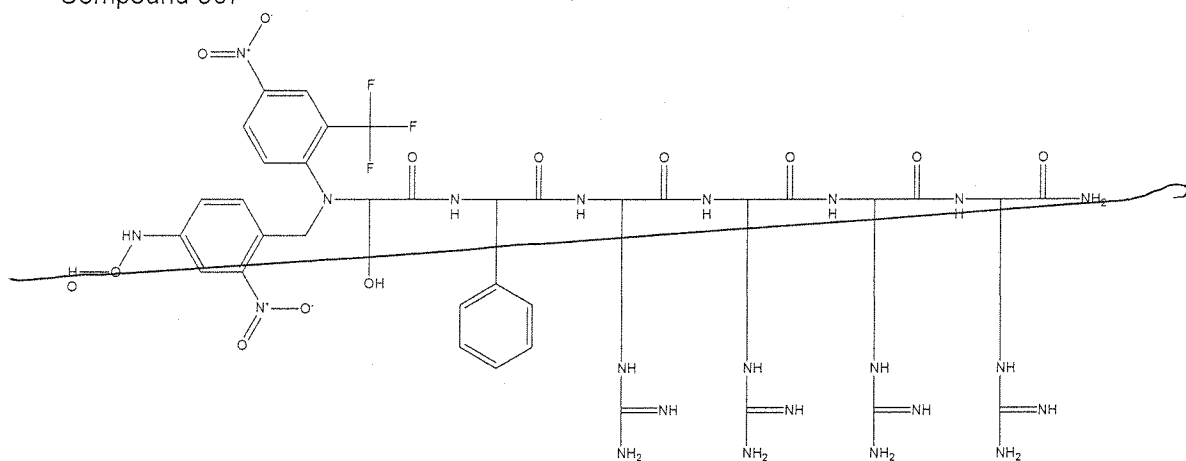


Compound 356

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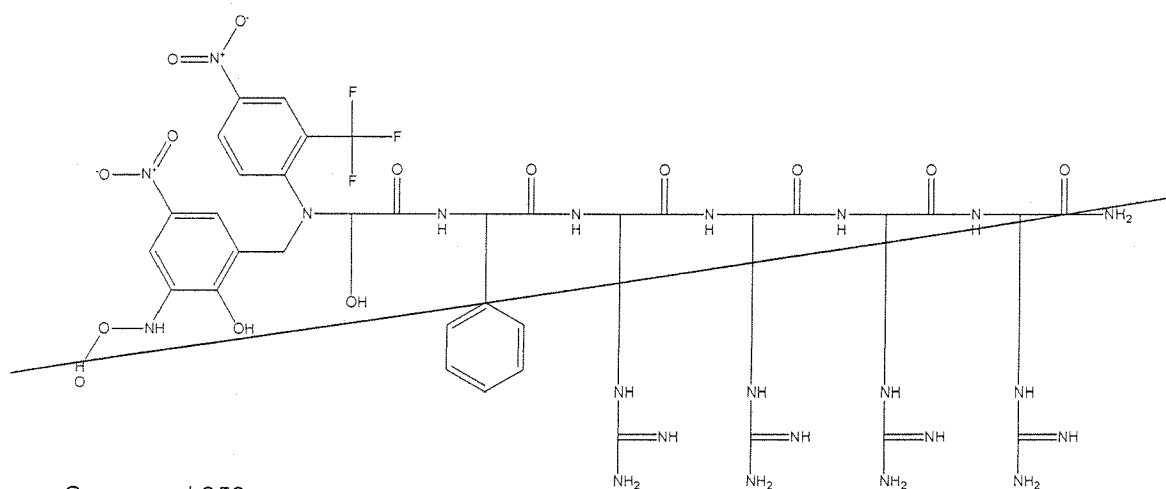


Compound 357

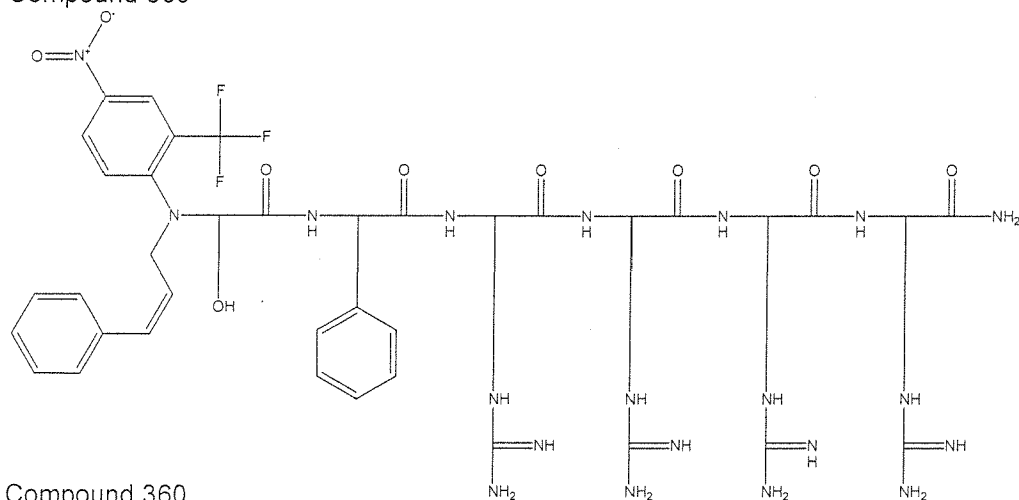


Compound 358

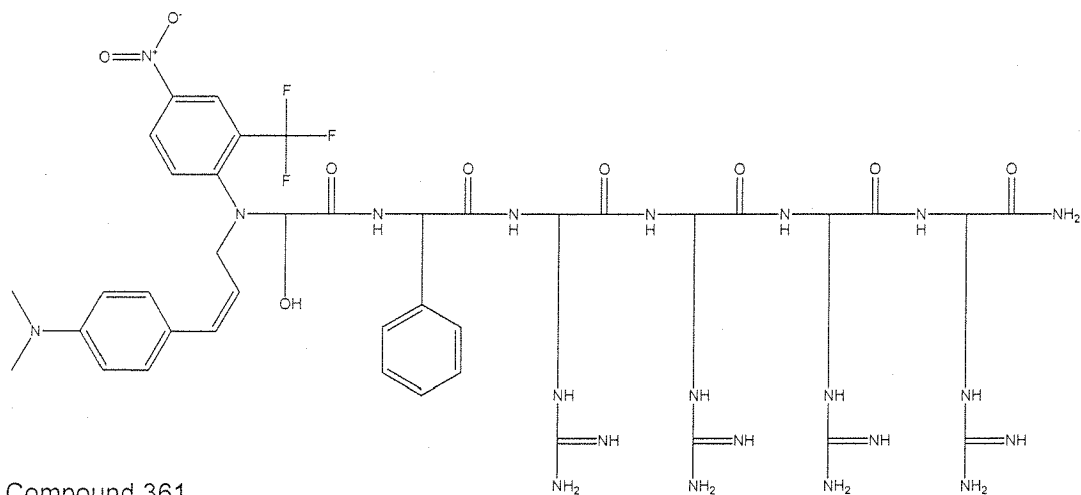
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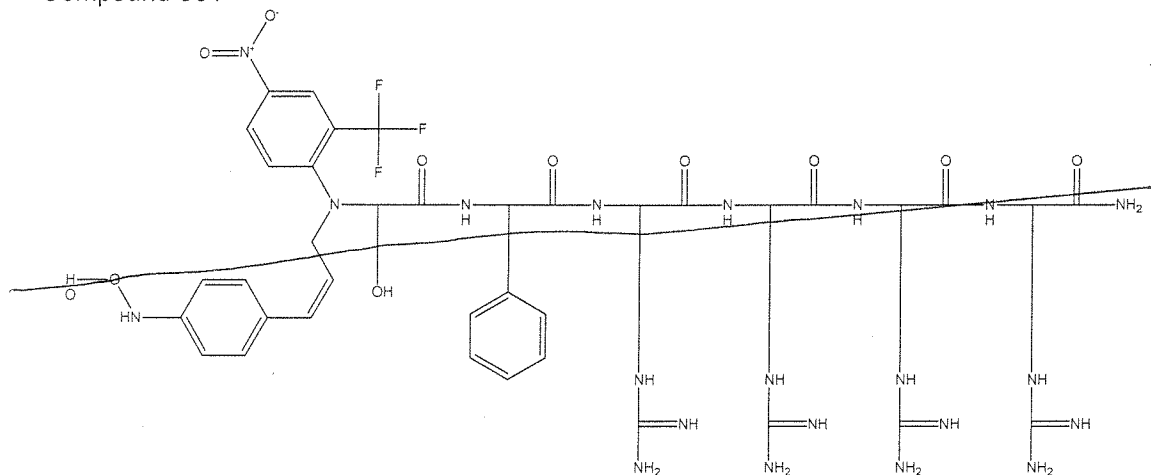
Compound 359



Compound 360

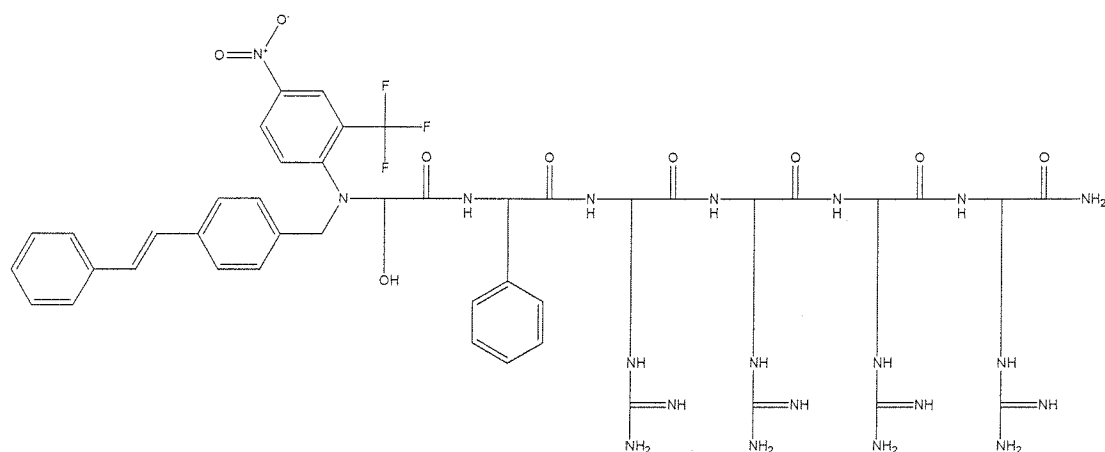


Compound 361

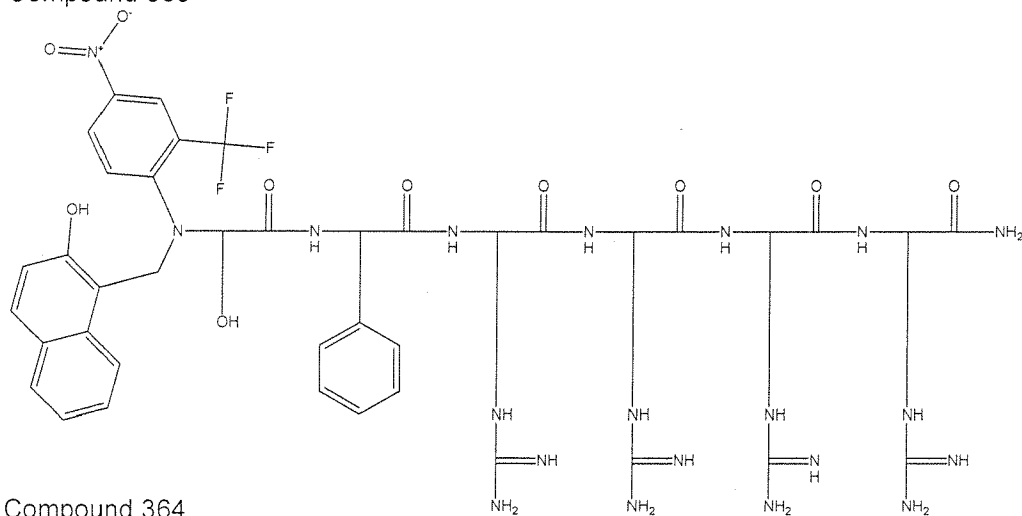


Compound 362

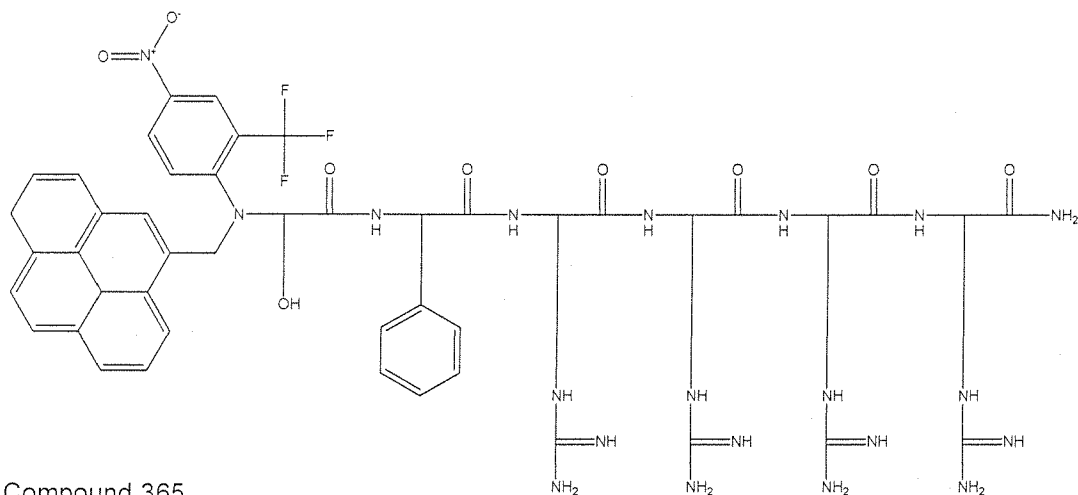
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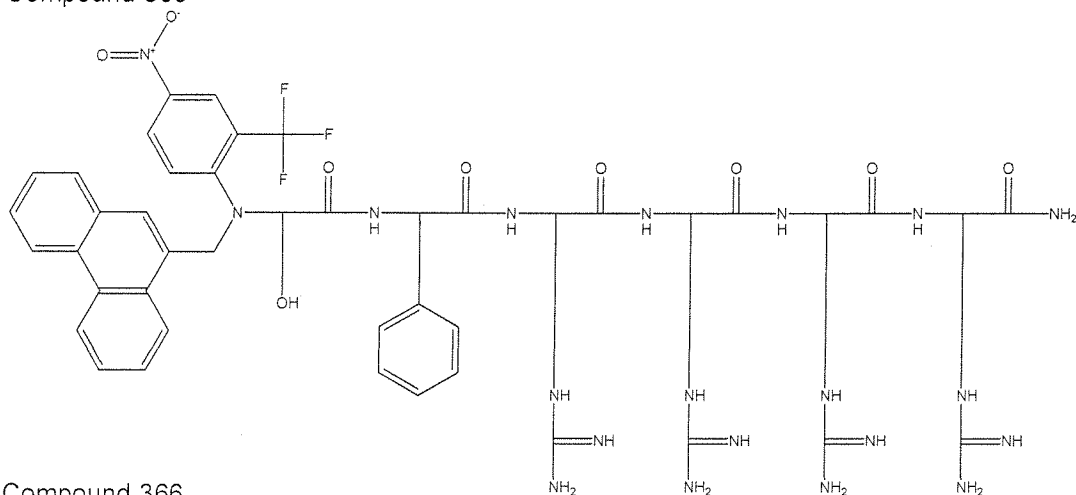
Compound 363



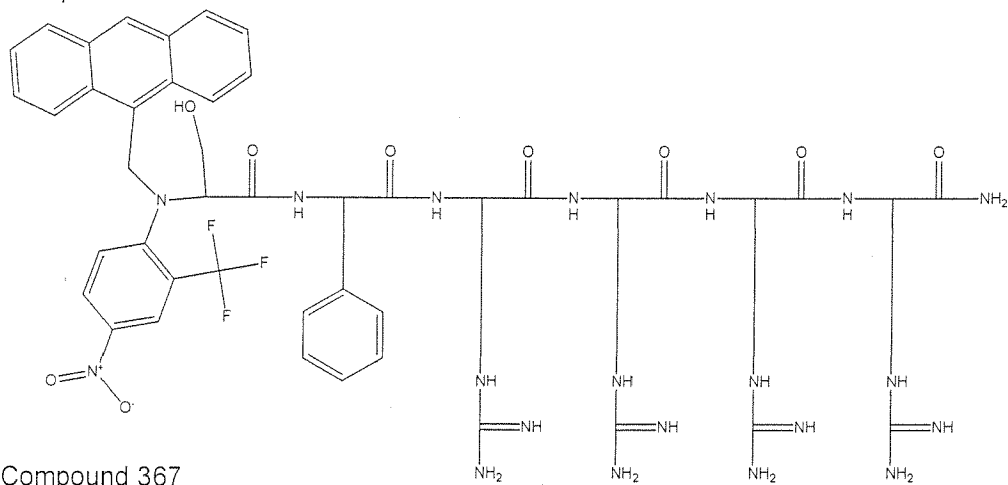
Compound 364



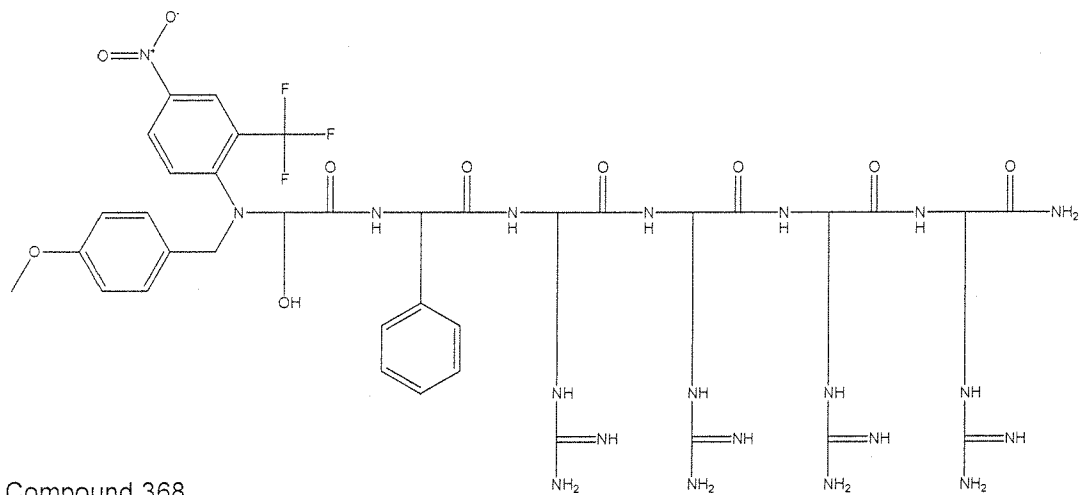
Compound 365



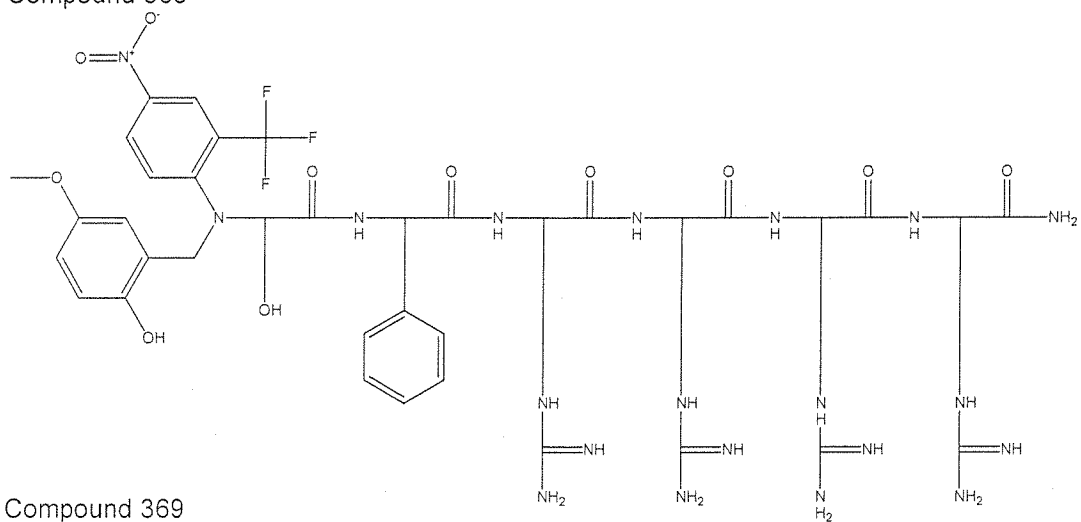
Compound 366



Compound 367

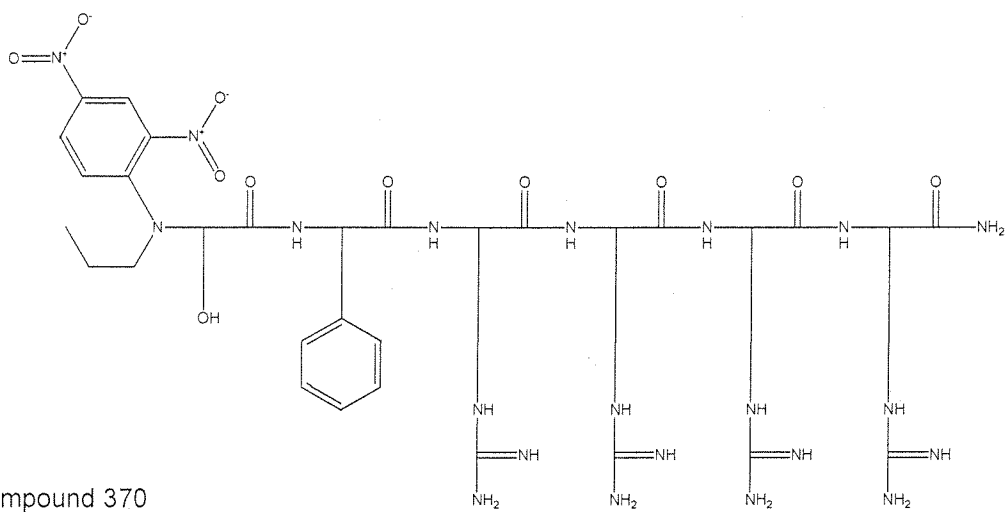


Compound 368

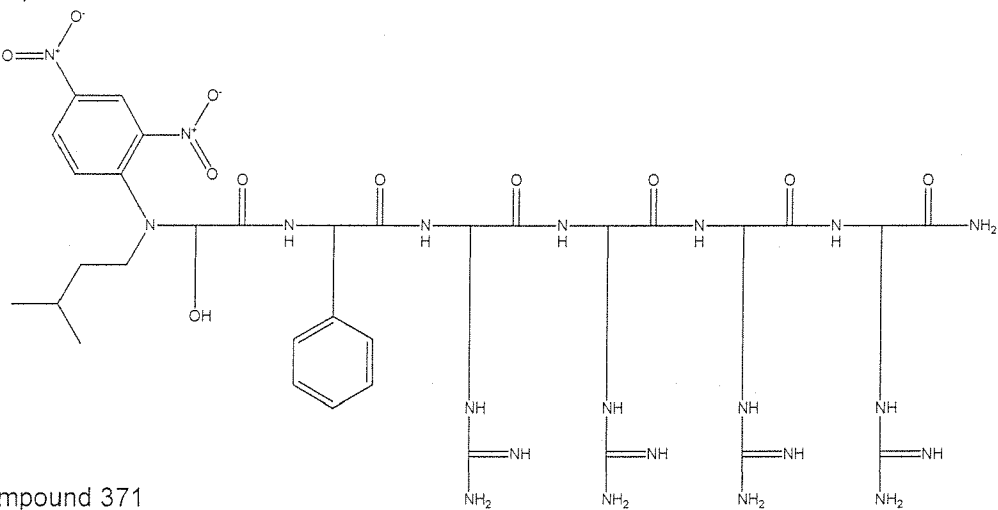


Compound 369

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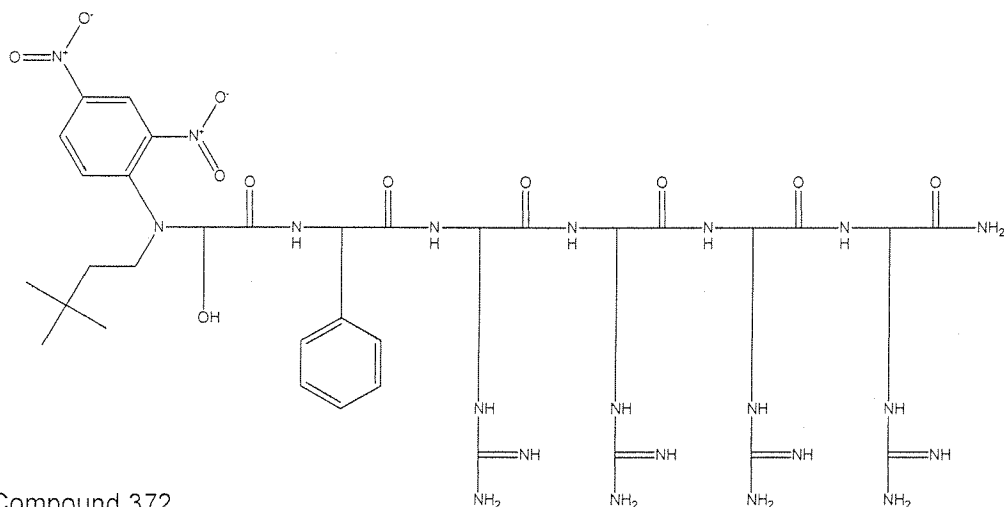


Compound 370

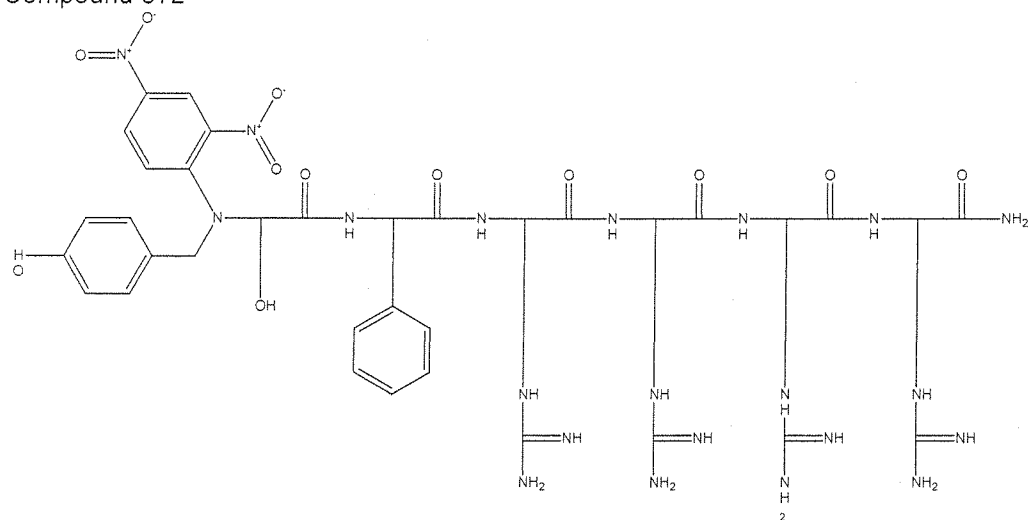


Compound 371

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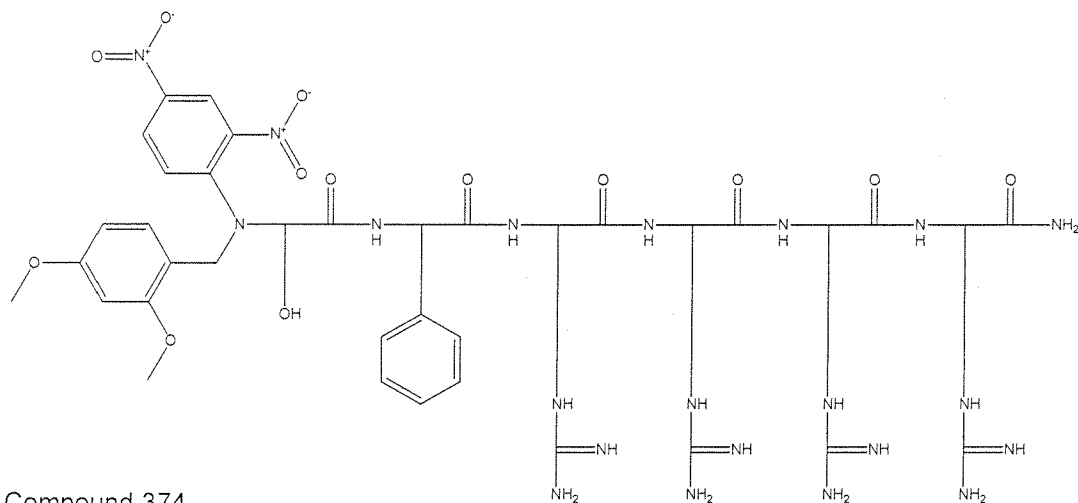


Compound 372

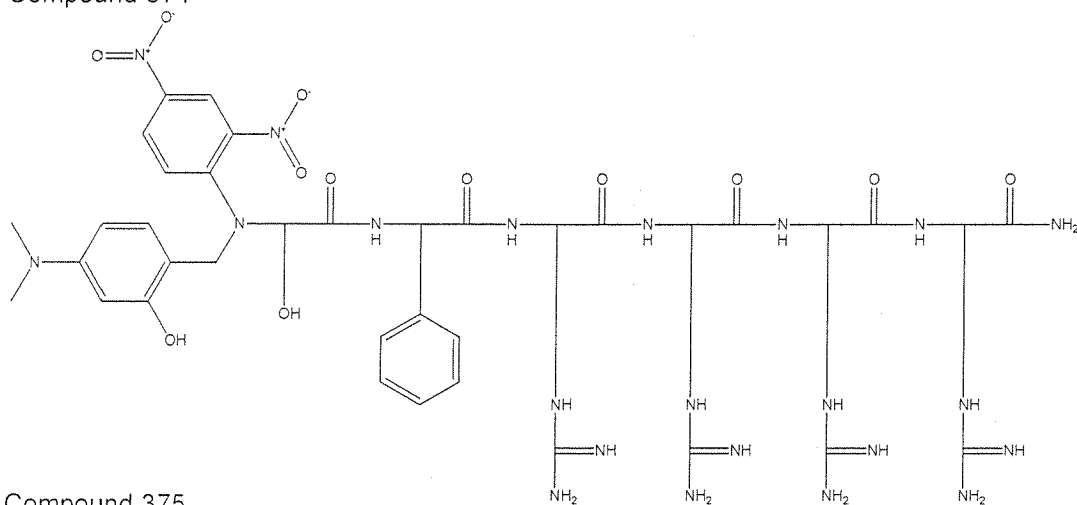


Compound 373

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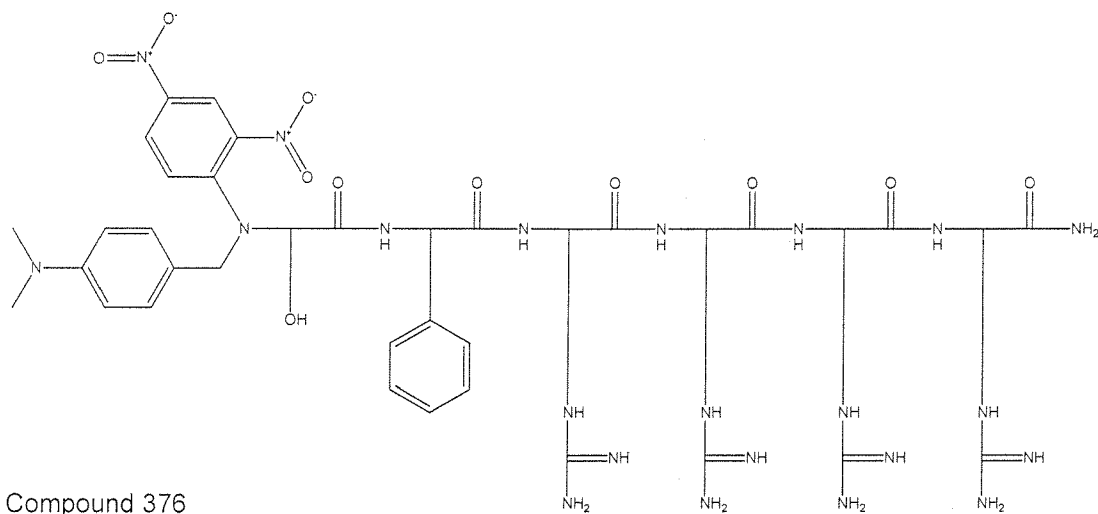


Compound 374

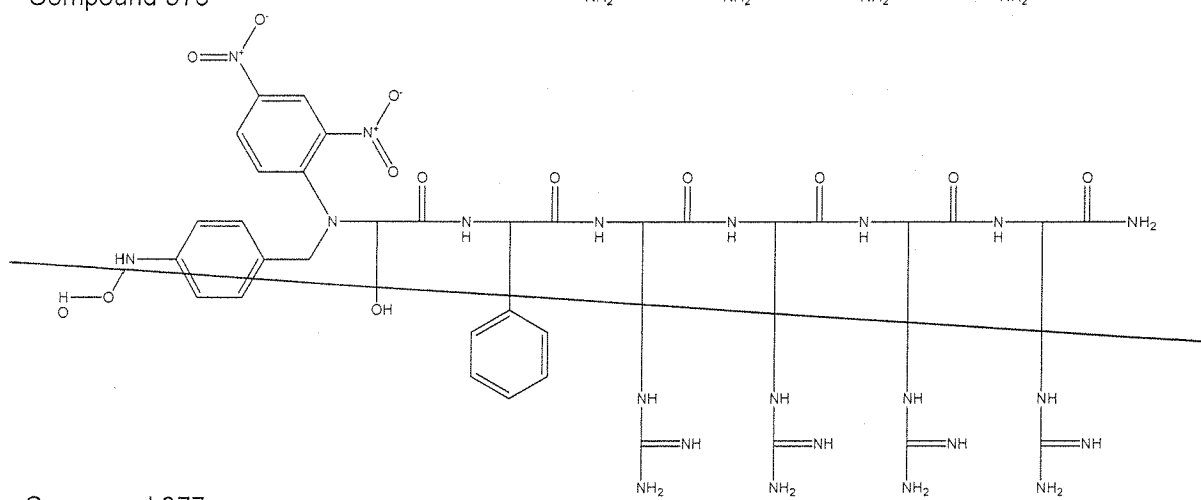


Compound 375

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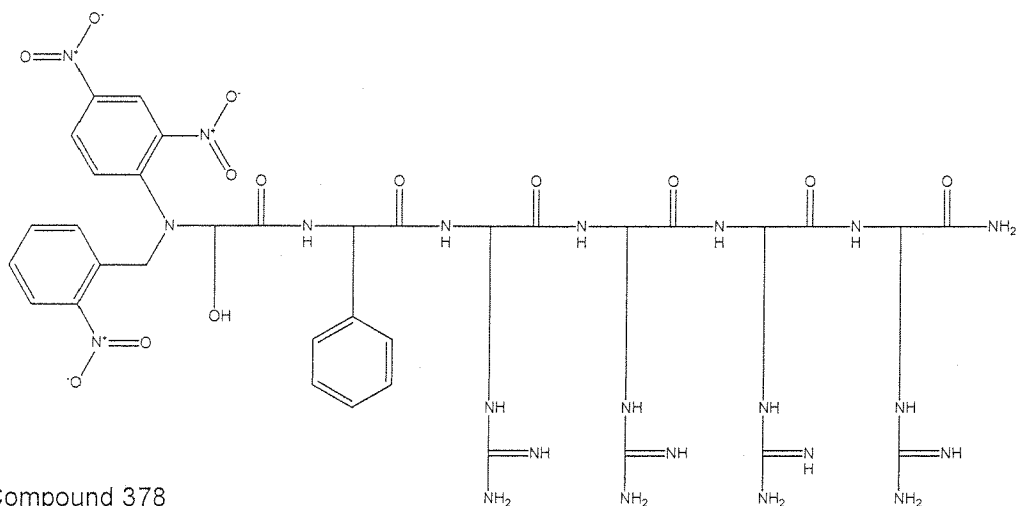


Compound 376

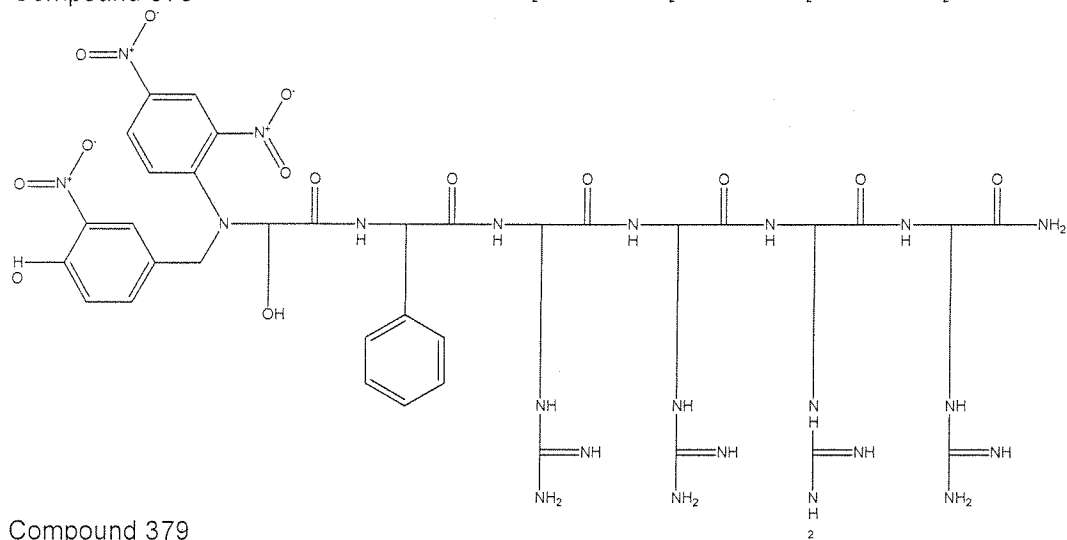


Compound 377

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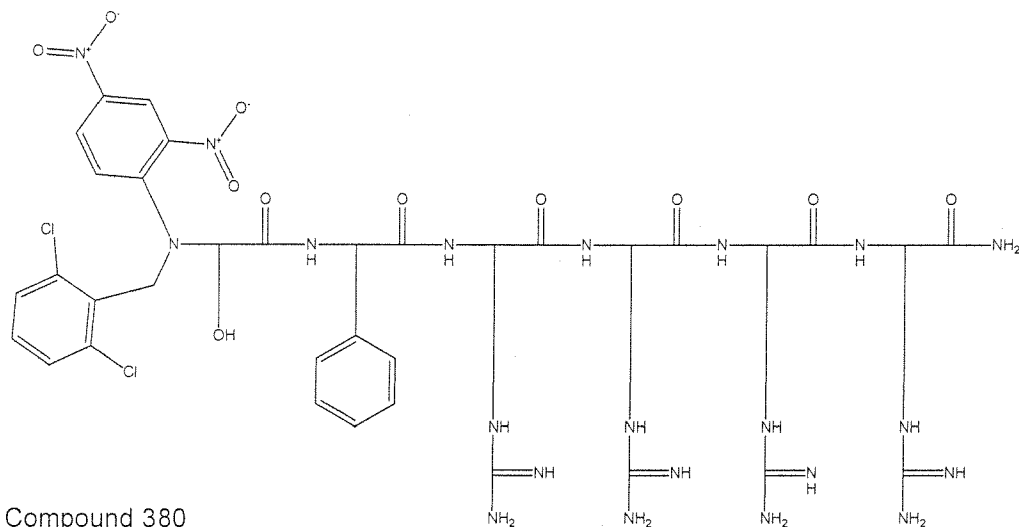


Compound 378

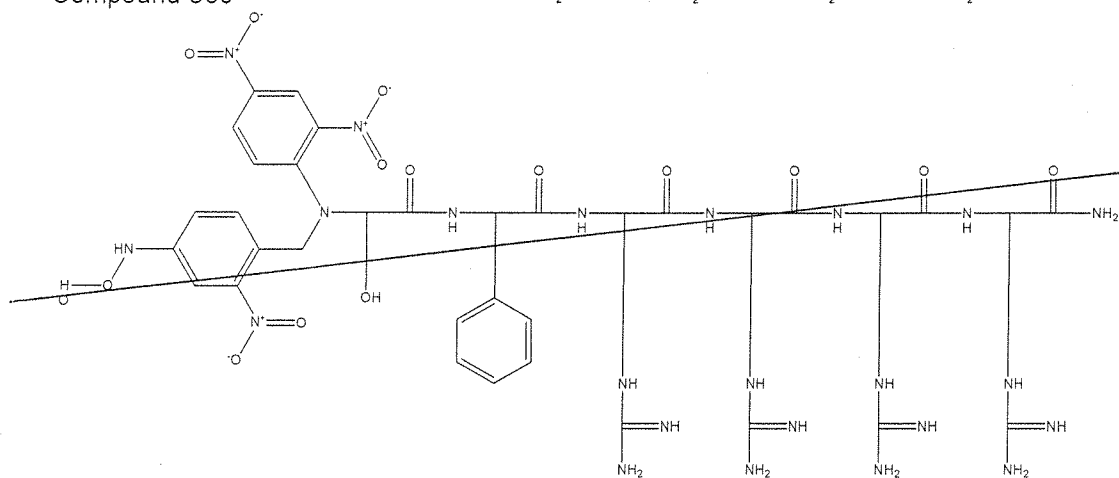


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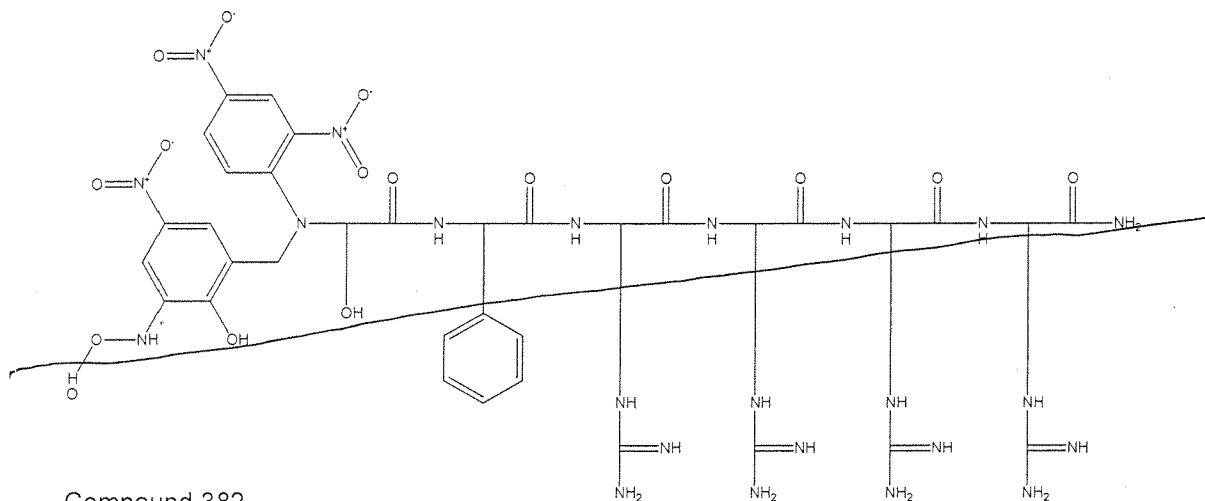


Compound 380

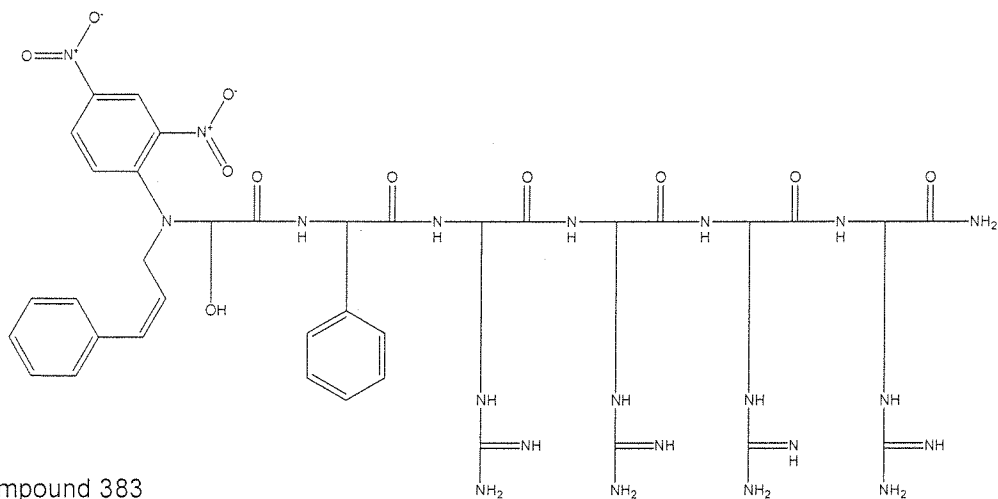


Compound 381

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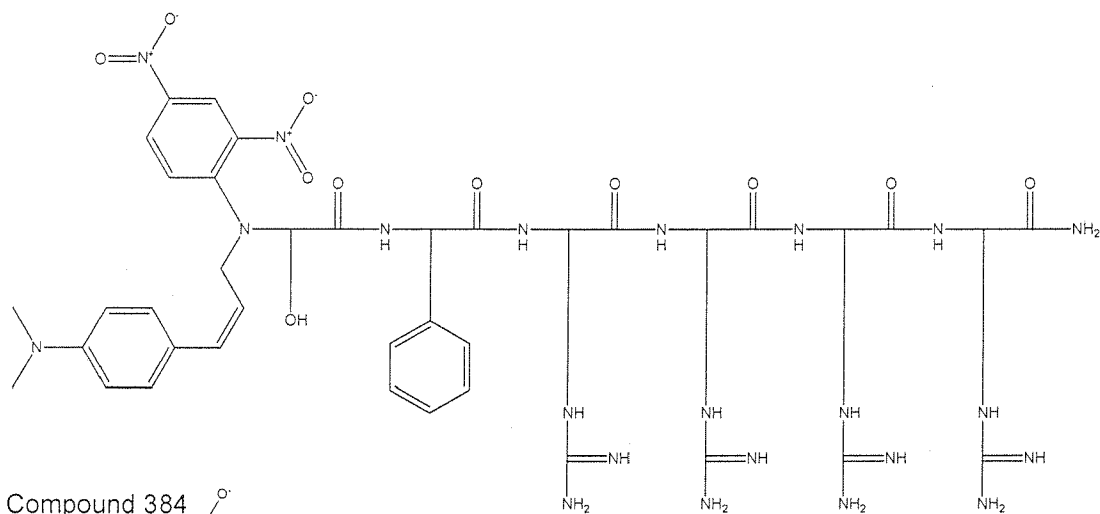


Compound 382

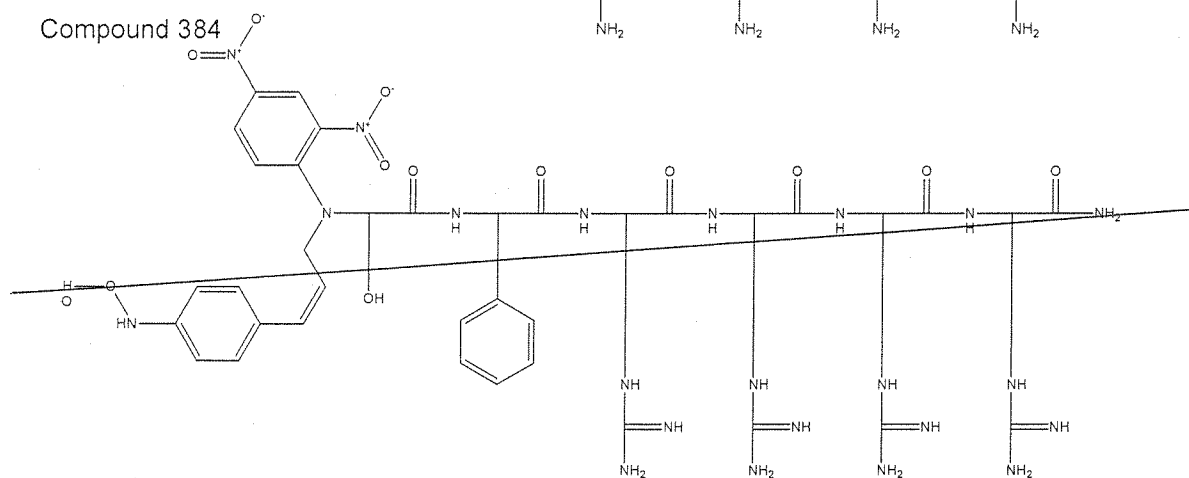


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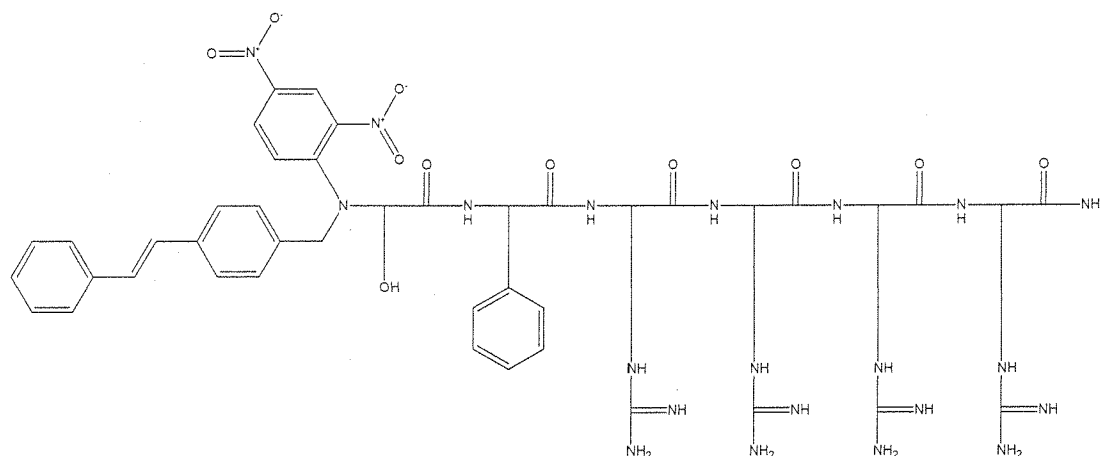


Compound 384

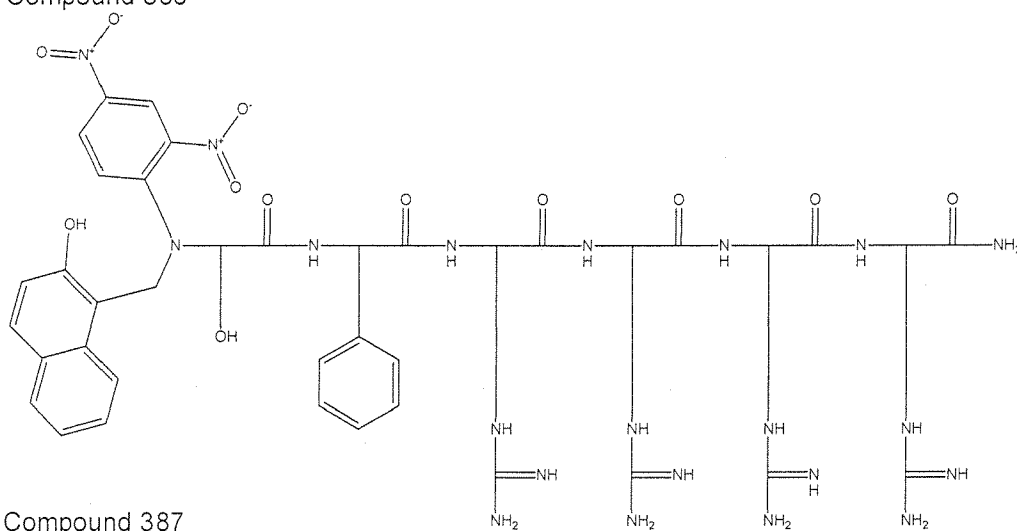


Compound 385

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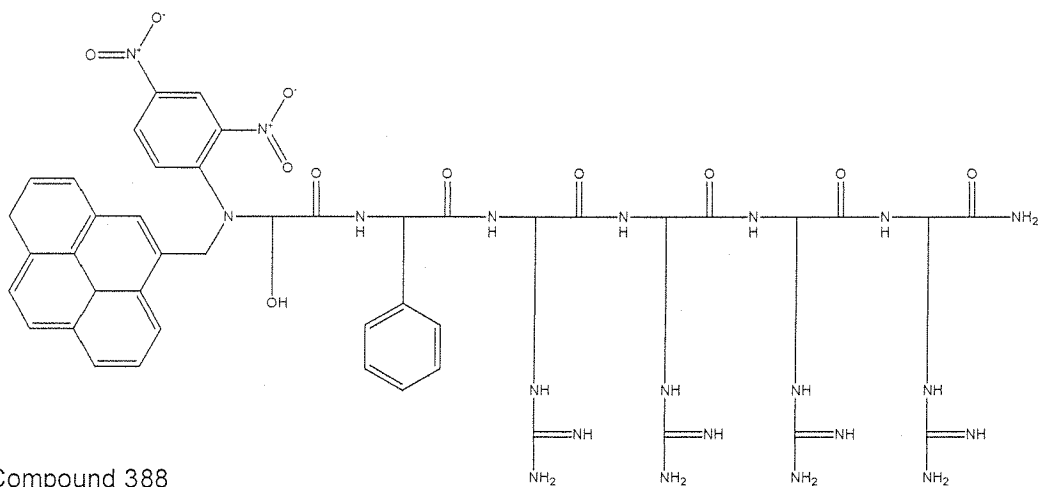


Compound 386

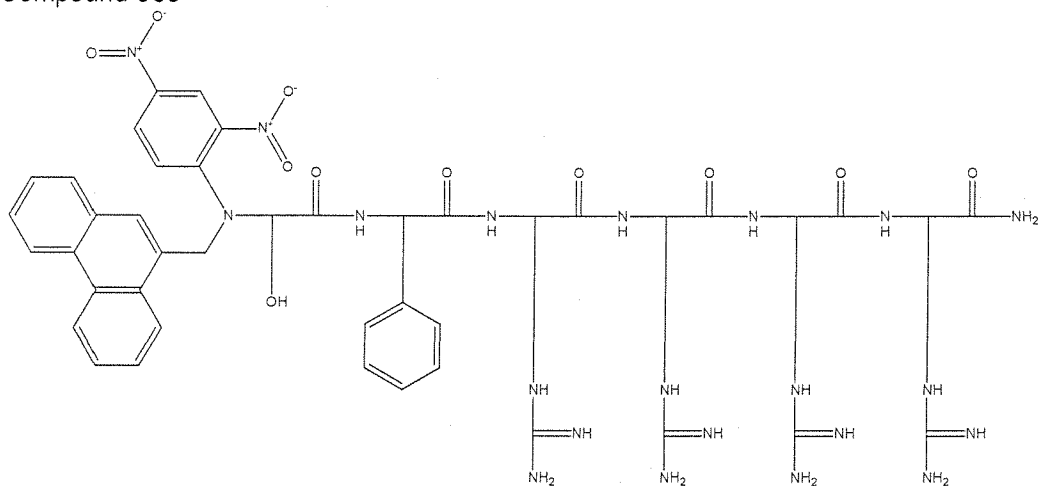


Compound 387

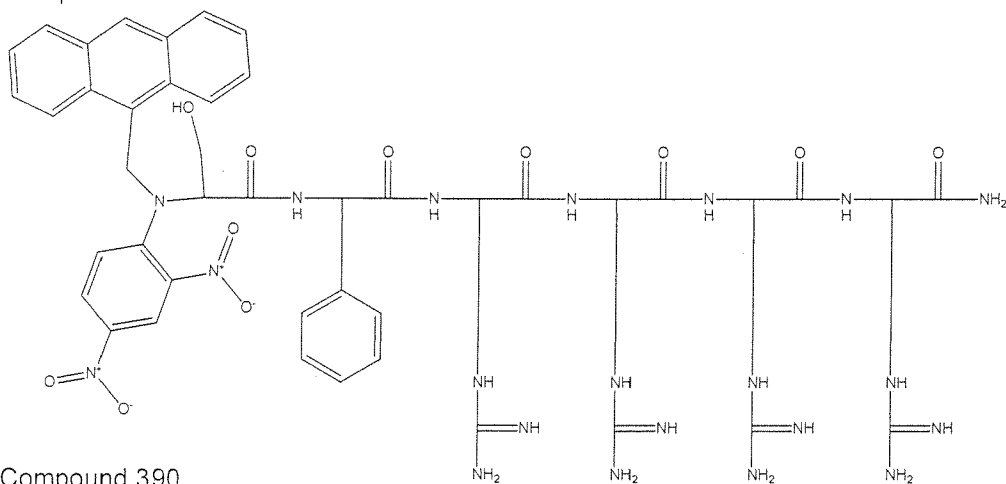
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Compound 388

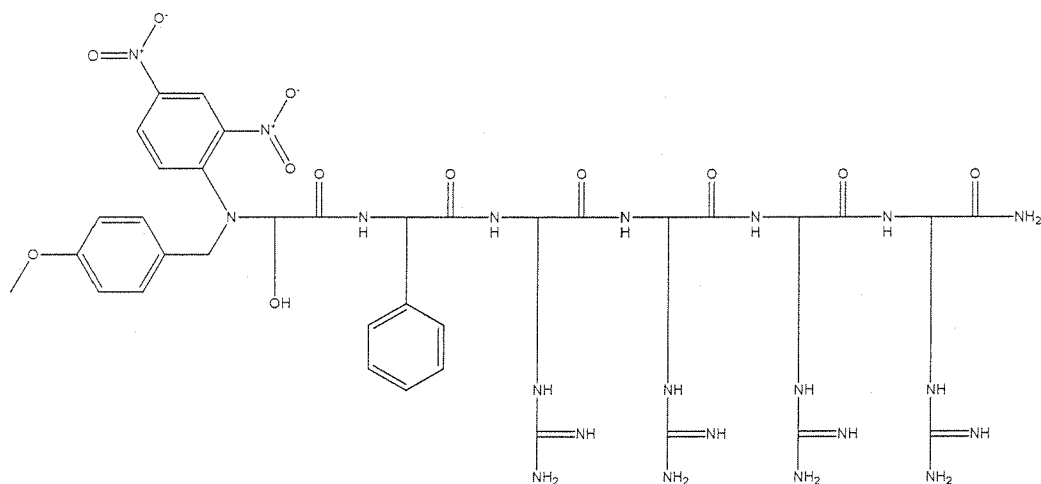


Compound 389

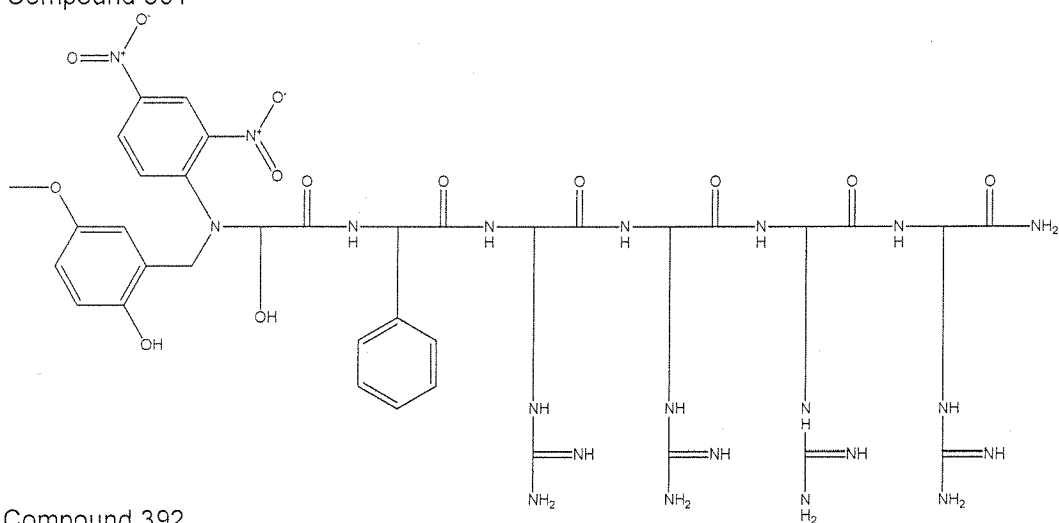


Compound 390

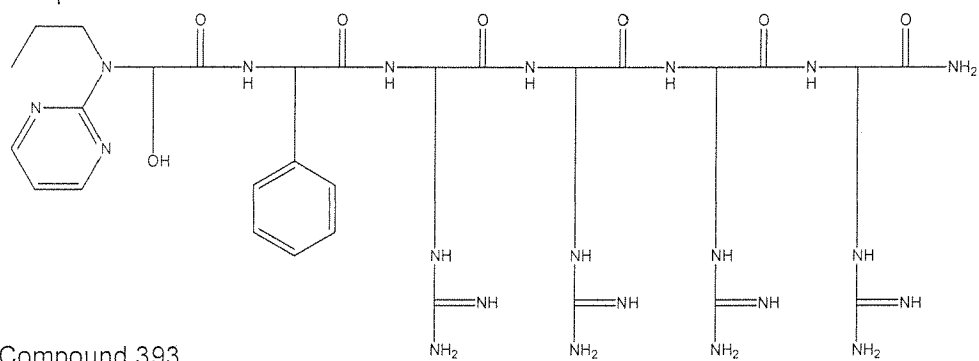
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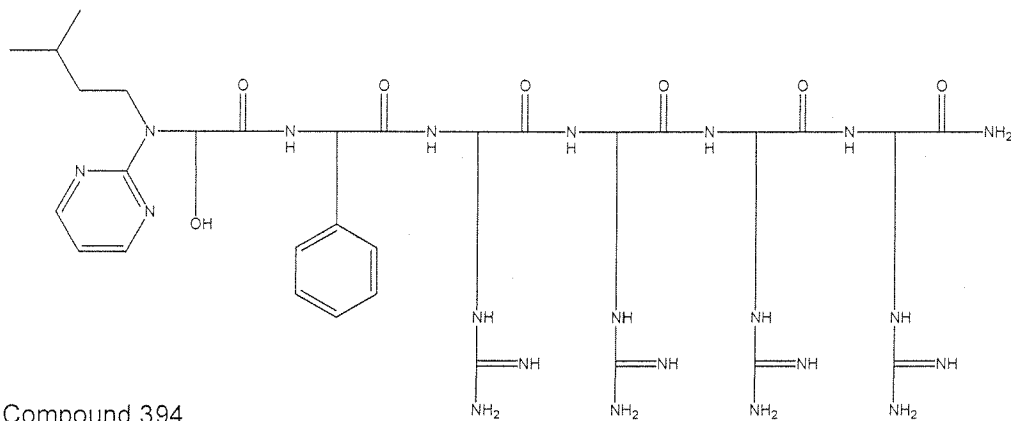
Compound 391



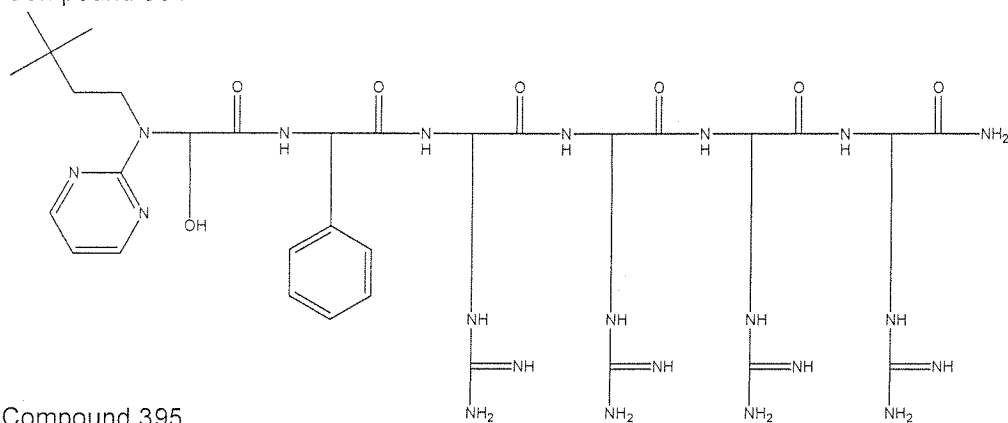
Compound 392



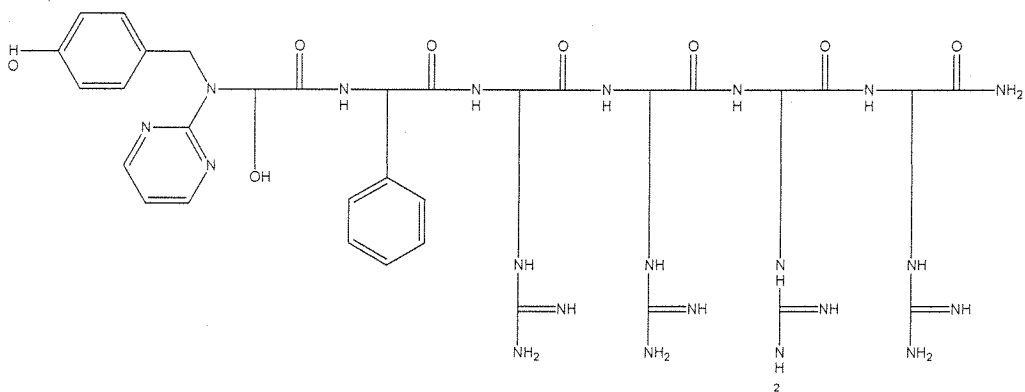
Compound 393



Compound 394

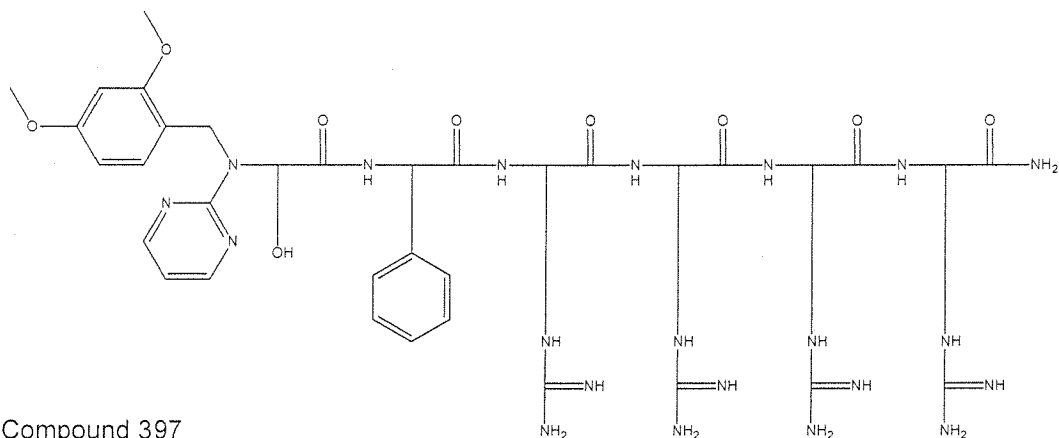


Compound 395

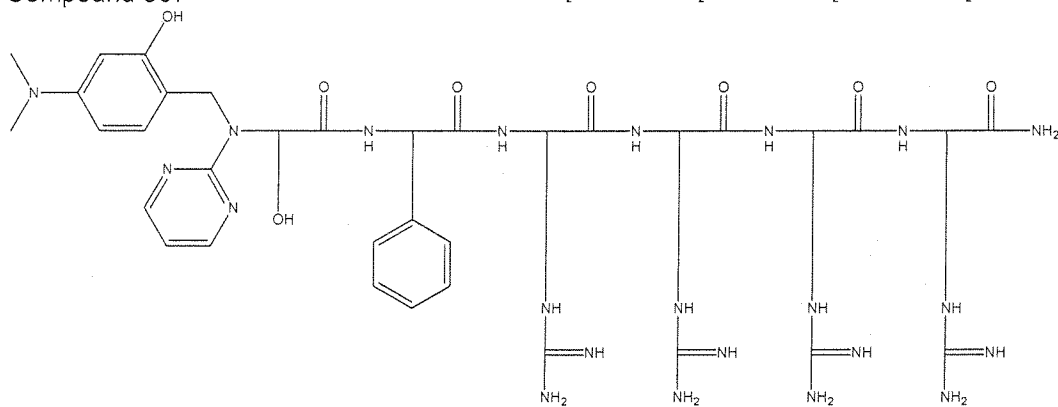


Compound 396

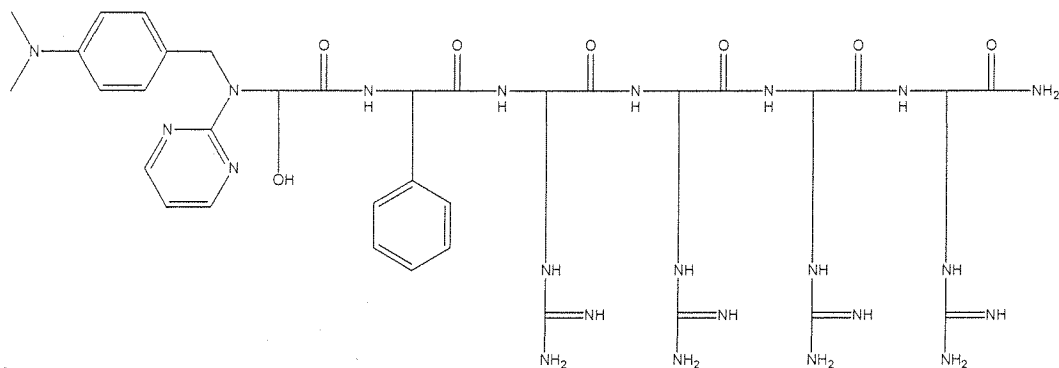
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Compound 397

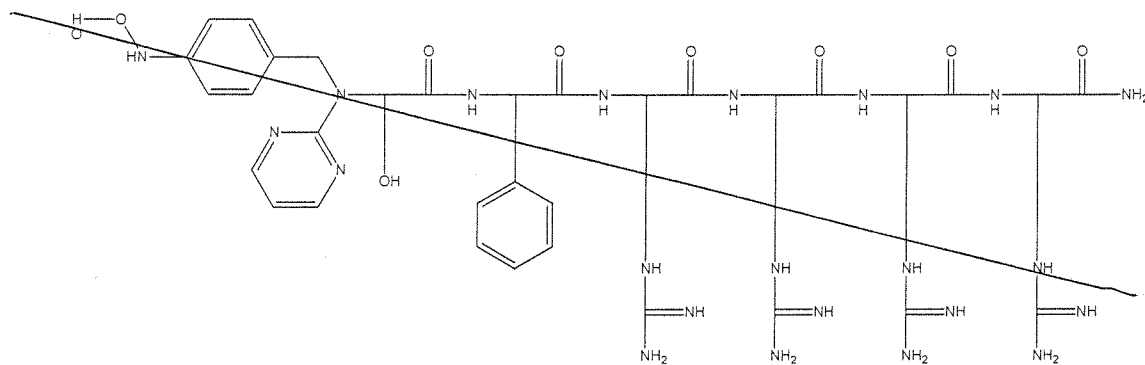


Compound 398

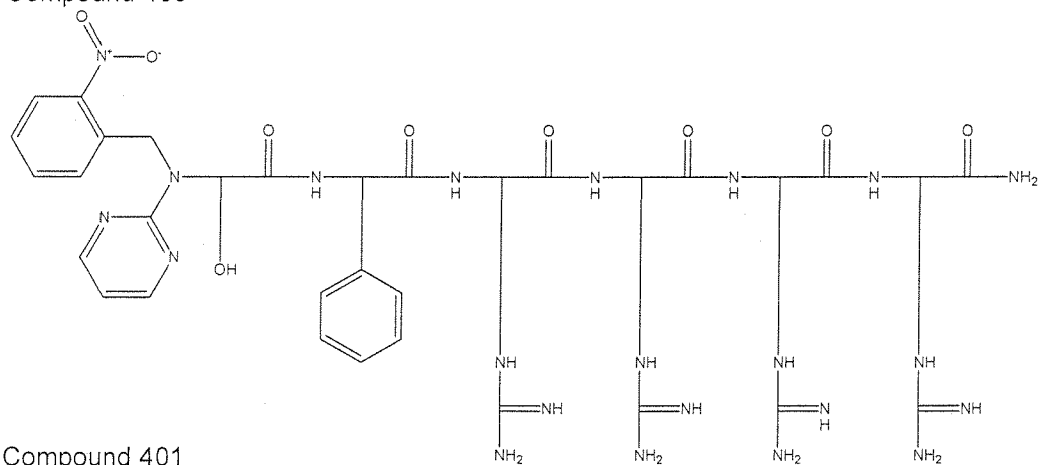


Compound 399

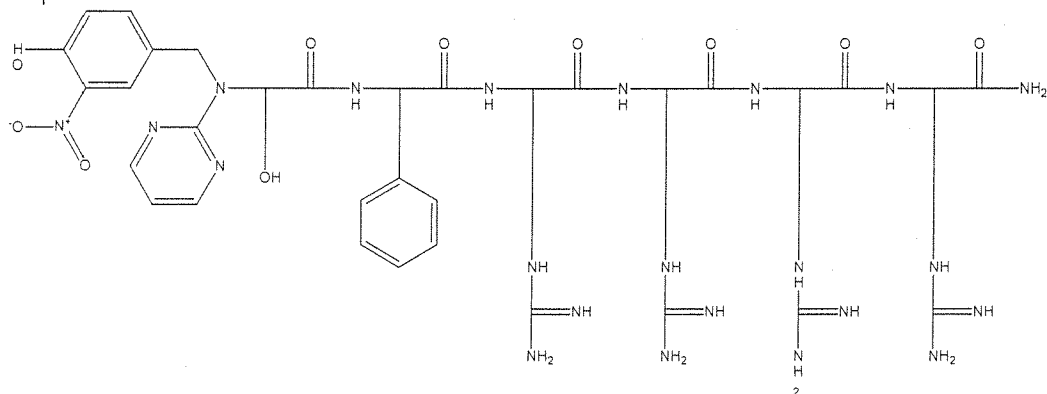
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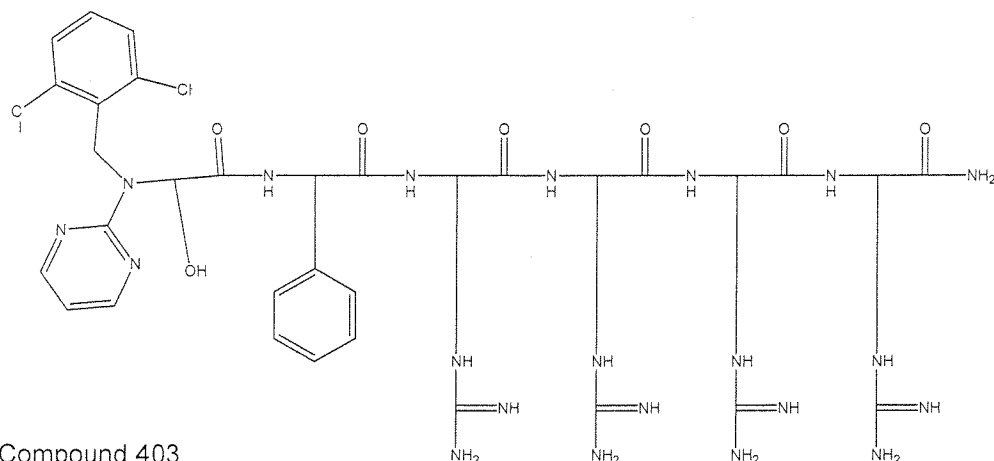
Compound 400



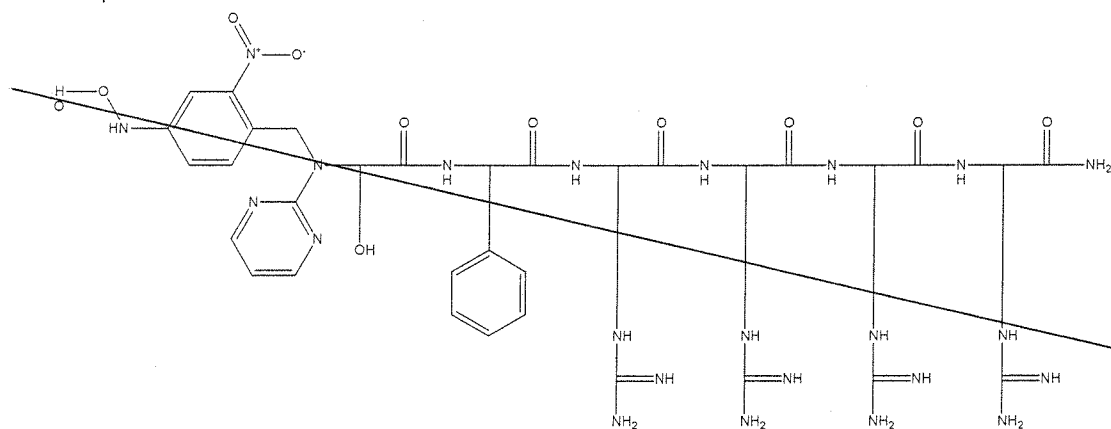
Compound 401



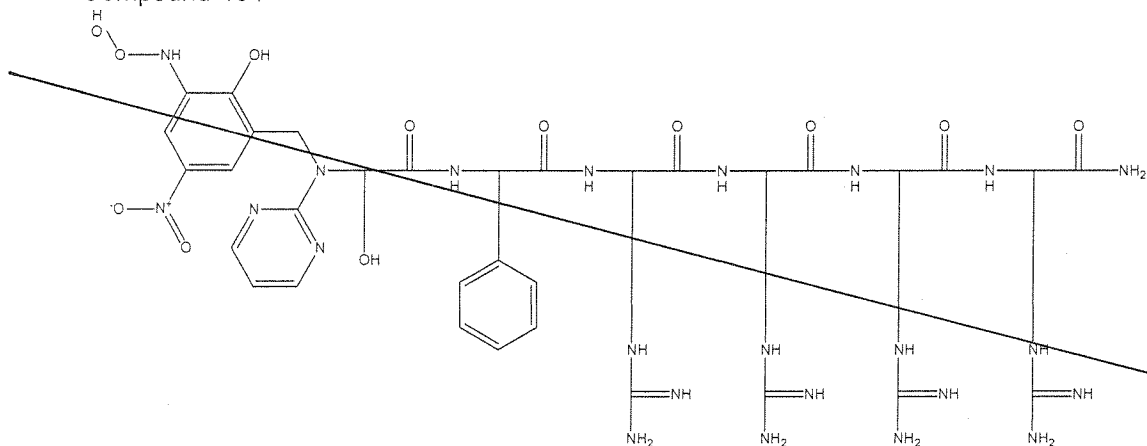
Compound 402



Compound 403

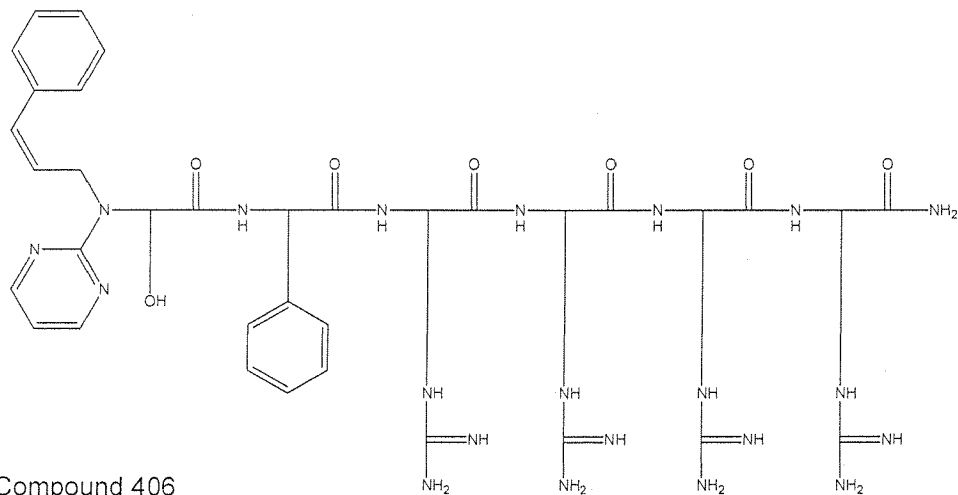


Compound 404

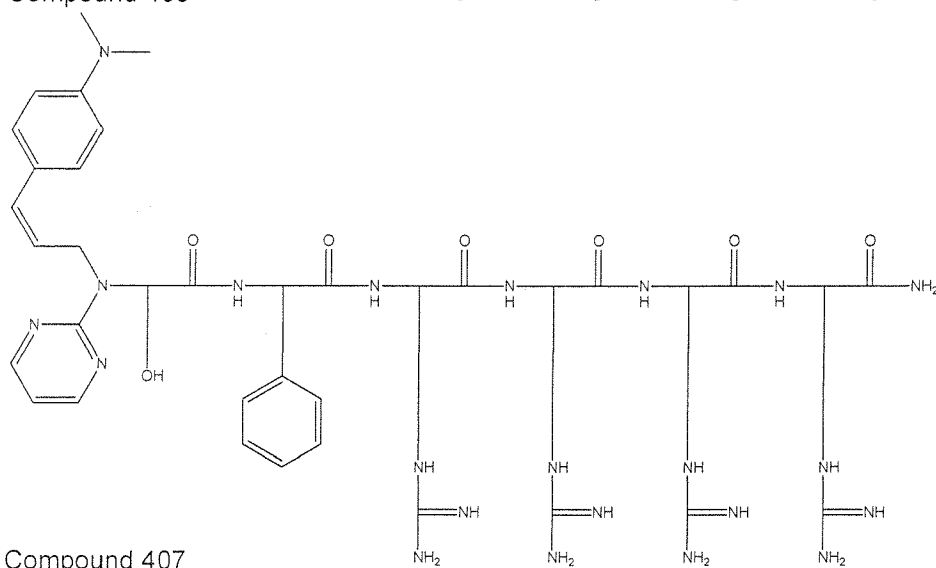


Compound 405

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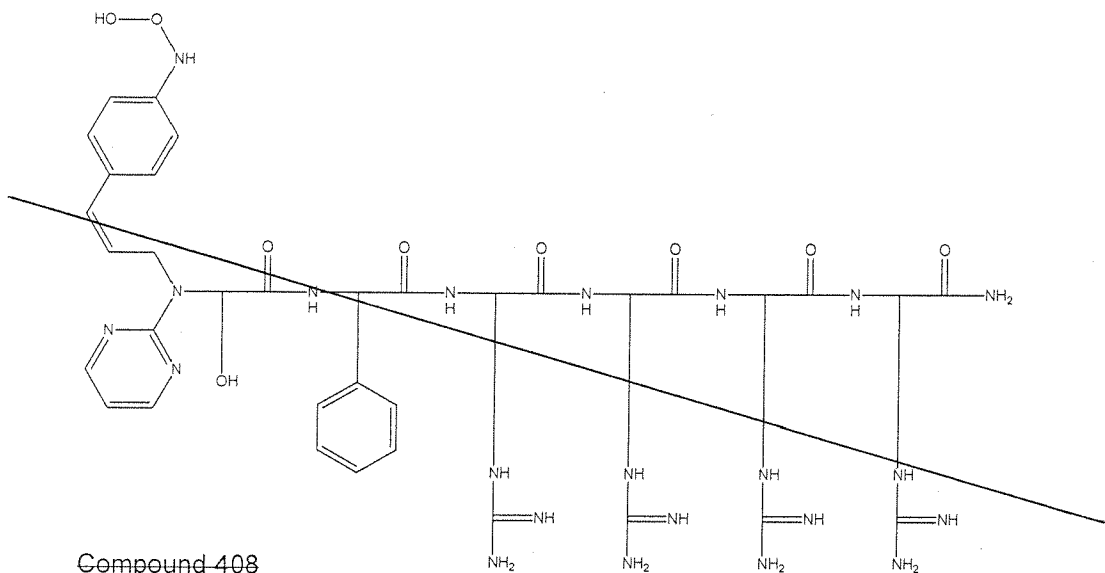


Compound 406

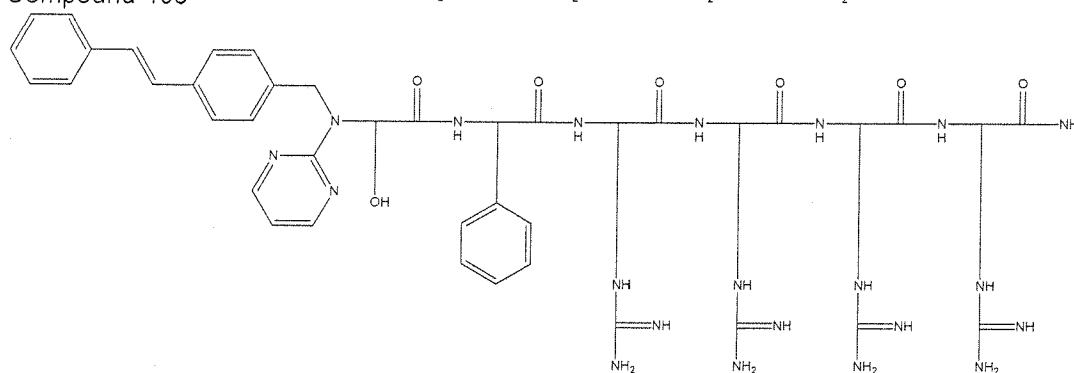


Compound 407

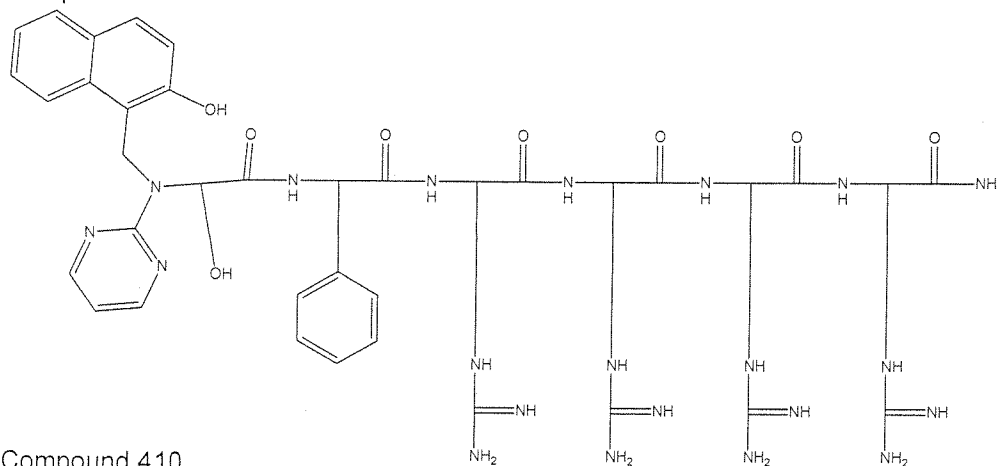
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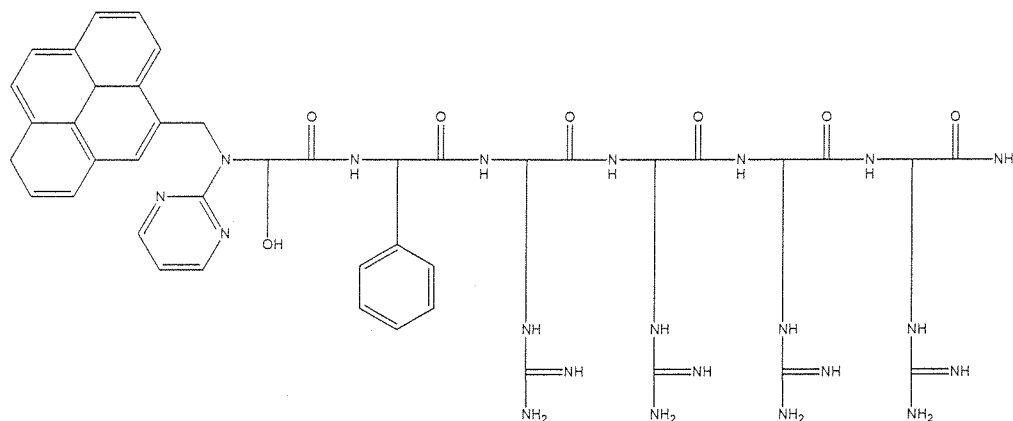
Compound 408



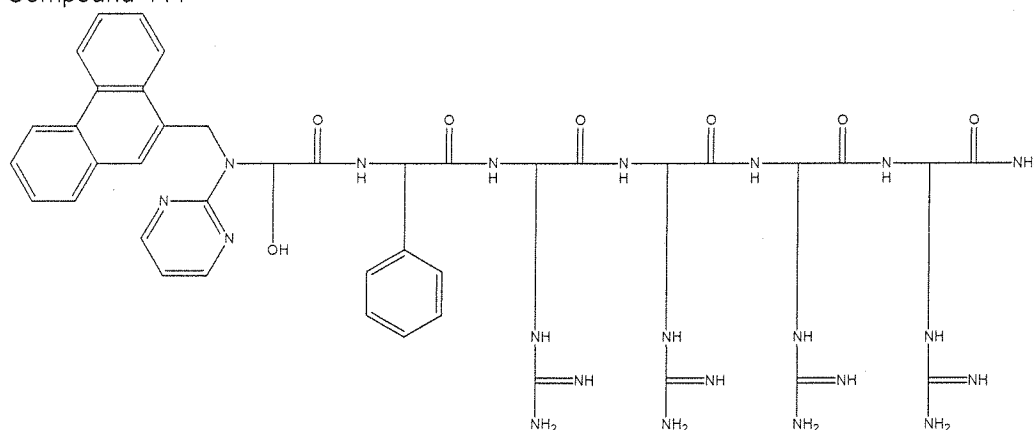
Compound 409



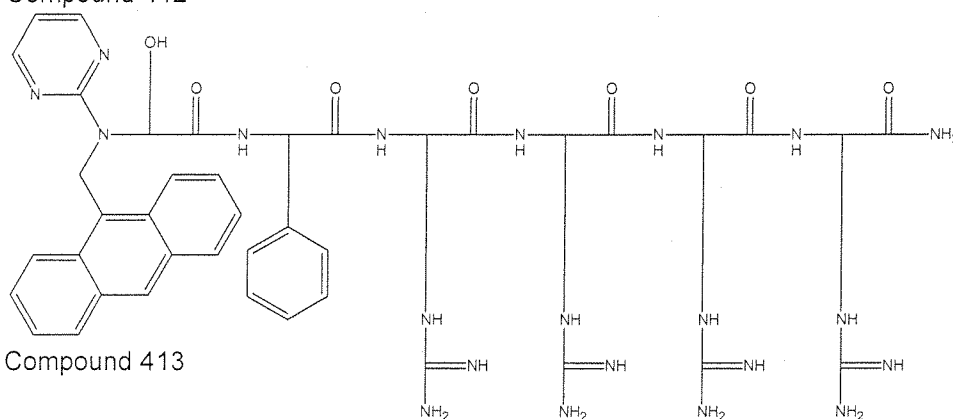
Compound 410



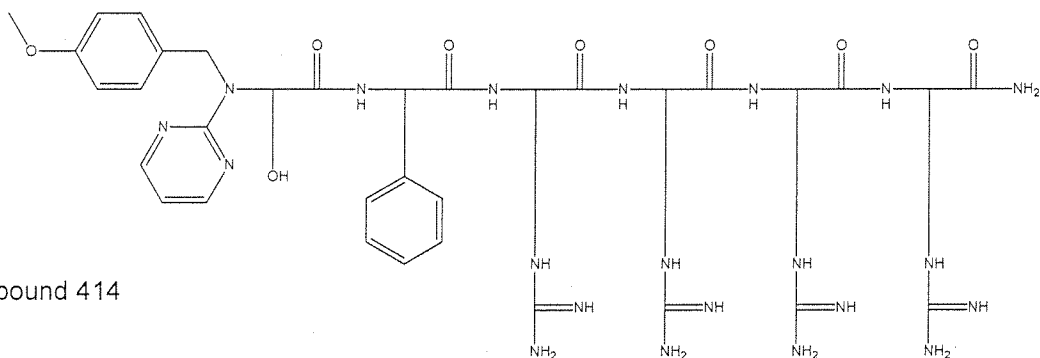
Compound 411



Compound 412

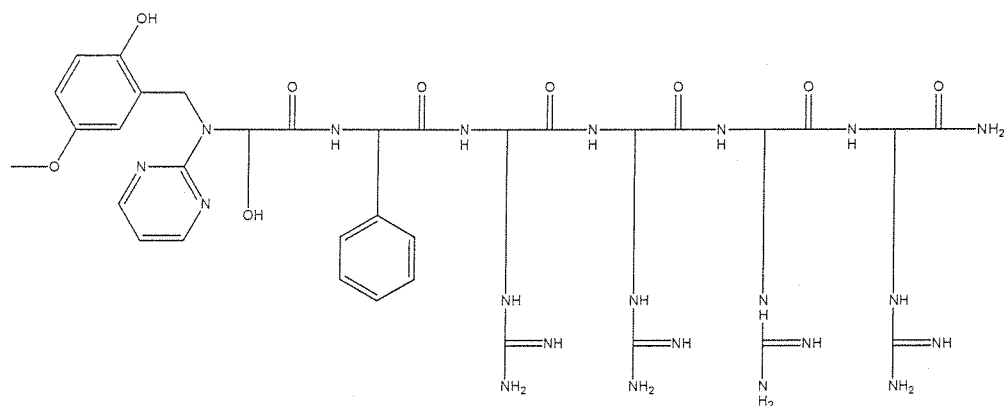


Compound 413



Compound 414

and



Compound 415

wherein amino acid chains are indicated as follows:

-OH represents serine,

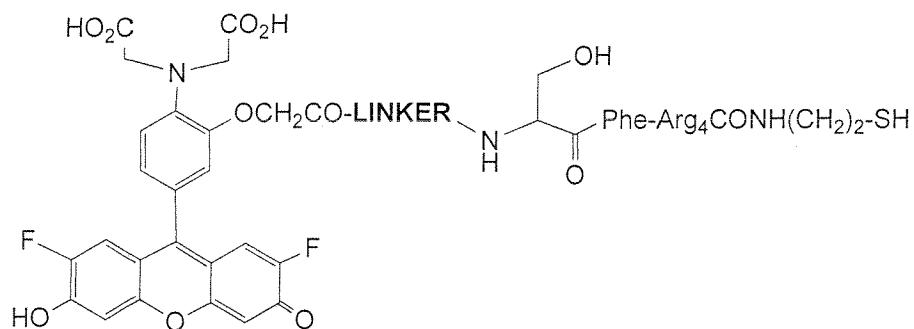
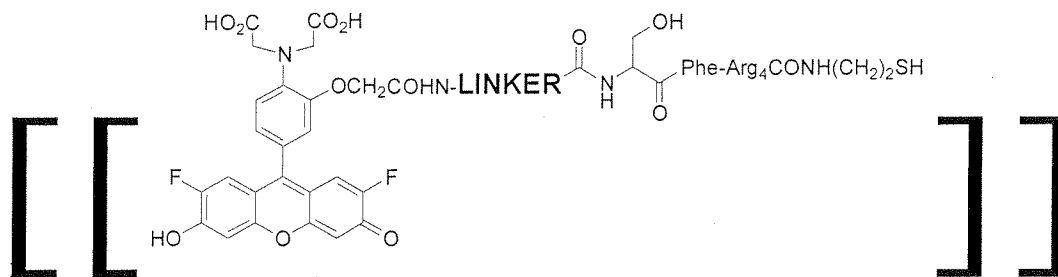
-NH₂ represents lysine,

—N—C(=NH)—NH₂ represents arginine, and

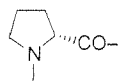
—C₆H₅ represents phenylalanine.

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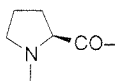
89. (Currently amended) A chemical compound comprising SEQ ID NO:1 having the structure:



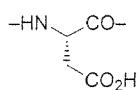
wherein the LINKER is selected from the group consisting of the following:



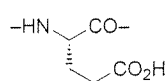
a



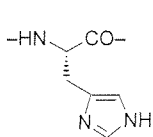
b



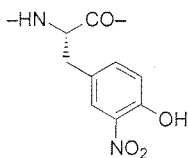
c



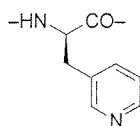
d



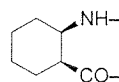
e



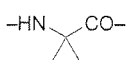
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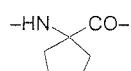
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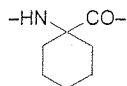
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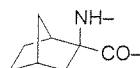
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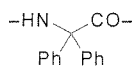
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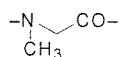
k



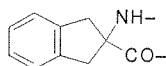
l



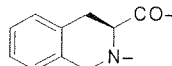
m



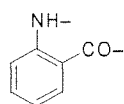
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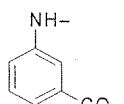
o



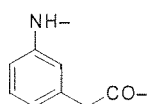
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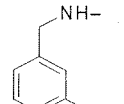
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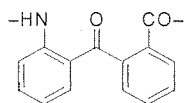
r



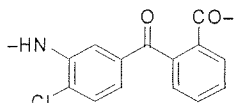
s



t



u



v

no linker

w

90. (Currently amended) A chemical compound having the structure: fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3); wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or tyrosine; ~~and~~ wherein the linker is selected from the group consisting of a carboxamide linker, an aminobenzoic acid linker, a sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an alkylamine linker, an arylamine linker, an ether linker, and a thioether linker; and wherein the chemical compound is a substrate for a protein kinase or a precursor of a substrate for a protein kinase.

91. (Original) The chemical compound of claim 90, wherein the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative.

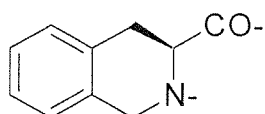
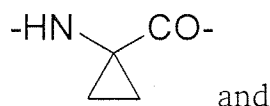
92. (Previously presented) The chemical compound of claim 90, wherein the fluorophore comprises a fluorescein group.

93. (Currently amended) The chemical compound of claim 90, wherein the fluorophore comprises a dansyl group, an acridine group, an Alexa Fluor® group, a BODIPY® group, an Oregon Green® group, a Rhodamine Green group, a Rhodamine Red-X group, a Texas Red® group, a Cascade Blue® group, a Cascade Yellow group, a Marina Blue® group, a Pacific Blue group, an AMCA-X group, or a coumarin group.

94-95. (Canceled)

96. (Previously presented) A chemical compound having the structure: fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3); wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or

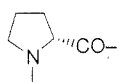
tyrosine, wherein the linker is selected from the group consisting of N-methyl glycine, L-proline, D-proline,



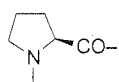
97. (Previously presented) A chemical compound having the structure:

fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3);

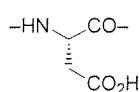
wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or tyrosine, wherein the linker is selected from the group consisting of the following:



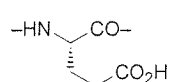
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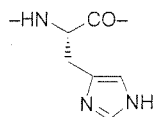
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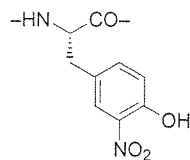
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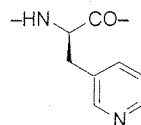
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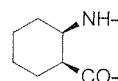
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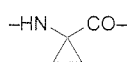
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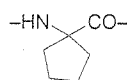
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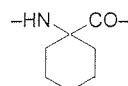
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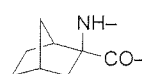
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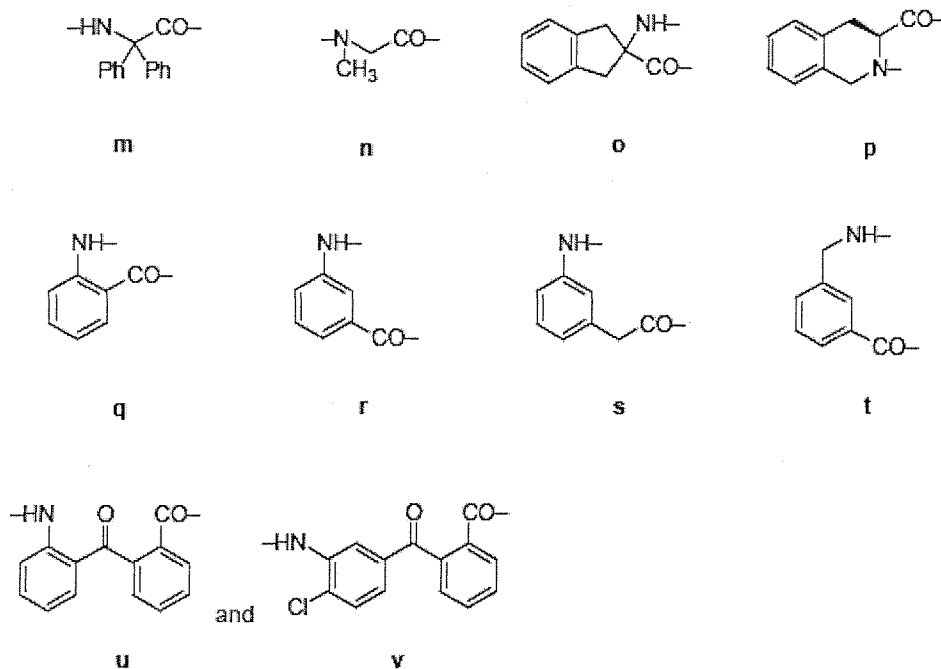
j



k



l



98. (Canceled)

99. (Currently amended) The chemical compound of claim 98 90, wherein the chemical compound is specific for protein kinase C.

100. (Original) The chemical compound of claim 99, wherein the chemical compound is specific for isoforms α , β , and γ of protein kinase C.

101. (Currently amended) The chemical compound of claim 98 90, the chemical compound is specific for protein kinase A, protein kinase B, protein kinase D, protein kinase G, Ca⁺/calmodulin-dependent protein kinase, mitogen-activated protein kinase,

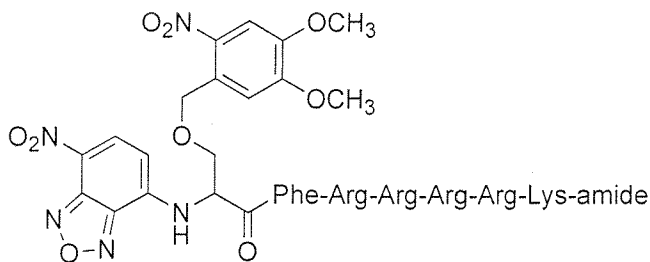
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protein kinase mos, protein kinase raf, protein tyrosine kinase, tyrosine kinase abl, tyrosine kinase src, tyrosine kinase yes, tyrosine kinase fps, tyrosine kinase met, cyclin-dependent protein kinase, or cdc2 kinase.

102. (Original) The chemical compound of claim 90, wherein the chemical compound further comprises a carbohydrate, a lipid or a nucleic acid.

103-121. (Canceled)

122. (Previously presented) A chemical compound comprising SEQ ID NO:3 having the structure



123. (Previously presented) A composition comprising a chemical compound of claim 89, and a carrier.

124-126. (Canceled)

127. (Currently amended) The precursor of a substrate for a protein kinase of claim 60, wherein the substrate comprises a metal ion chelator.

128. (Currently amended) The precursor of a substrate for a protein kinase of claim 127, wherein the metal ion is a magnesium ion or a calcium ion.

129. (Currently amended) The chemical compound of claim 90, wherein the chemical compound comprises a metal ion chelator and the metal ion chelator induces a change in fluorescence intensity.

130. (Original) The chemical compound of claim 129, wherein the metal ion is a magnesium ion or a calcium ion.

131. (Original) The chemical compound of claim 129, wherein the change in fluorescence intensity is at least a 20% change in fluorescence intensity.

132. (Canceled)

133. (Previously presented) The chemical compound of claim 90, wherein the linker comprises a turn to position the fluorophore in a location closer to the serine, the threonine or the tyrosine than the location the fluorophore would occupy in the absence of a turn in the linker.

134. (Previously presented) The chemical compound of claim 89, wherein the linker comprises a turn to position the fluorophore in a location closer to the terminal serine, the terminal threonine or the terminal tyrosine than the location the fluorophore would occupy in the absence of a turn in the linker.

135-136. (Canceled)

137. (Previously presented) The composition of claim 123, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

138. (Previously presented) A composition comprising the substrate of claim 49, and a carrier.

139. (Previously presented) The composition of claim 138, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

140. (Previously presented) A composition comprising the compound of claim 88, and a carrier.

141. (Previously presented) The composition of claim 140, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

142. (Previously presented) A composition comprising the compound of claim 90, and a carrier.

143. (Previously presented) The composition of claim 142, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

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144-145. (Canceled)

146. (Previously presented) A composition comprising the compound of claim 122, and a carrier.

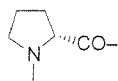
147. (Previously presented) The composition of claim 146, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

148. (Currently amended) A precursor of a substrate for a protein kinase ~~or a precursor of the substrate~~, wherein the ~~substrate or the precursor~~ comprises:

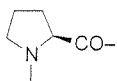
a peptide substrate for the protein kinase, wherein the peptide comprises a serine, a threonine, or a tyrosine on a terminal end of the peptide;

at least one fluorophore, wherein a fluorophore is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide;

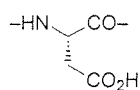
wherein the fluorophore is attached directly to the peptide or the fluorophore is attached to the peptide by a linker selected from the group consisting of



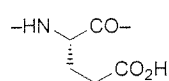
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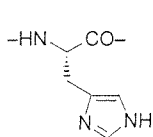
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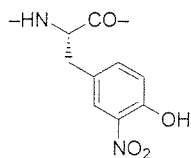
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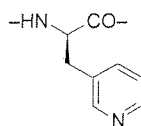
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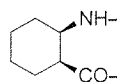
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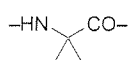
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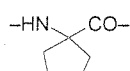
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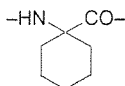
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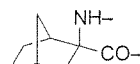
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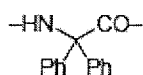
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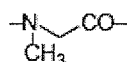
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l



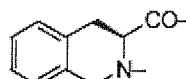
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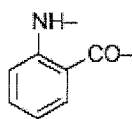
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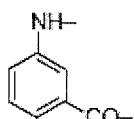
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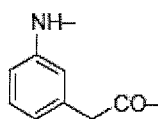
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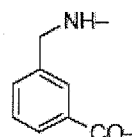
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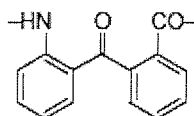
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s

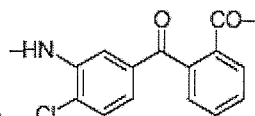


t



u

and



v

;

wherein a photolabile side chain is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide, and wherein the photolabile side chain blocks transfer of a phosphoryl group from adenosine triphosphate to a hydroxyl moiety of the serine, the threonine, or the tyrosine so that the precursor substrate cannot be phosphorylated by a protein kinase until the photolabile side chain is removed from the precursor substrate.

149. (Previously presented) A composition comprising the substrate of claim 83, and a carrier.

150. (Previously presented) The composition of claim 149, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

151. (Previously presented) A composition comprising the precursor of a substrate for a protein kinase of claim 59, and a carrier.

152. (Previously presented) The composition of claim 151, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

153. (Currently amended) A composition comprising the precursor of a substrate for a protein kinase ~~or a precursor of the substrate~~ of claim 148, and a carrier.

154. (Previously presented) The composition of claim 153, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.